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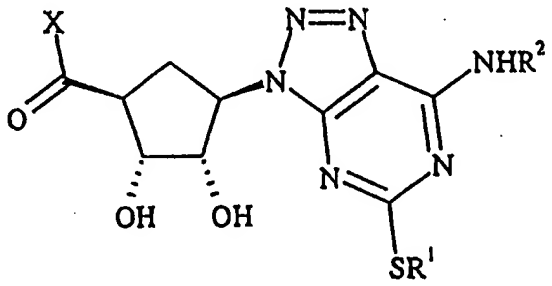
(54) Title: TRIAZOLO[4,5-*D*]PYRIMIDINYL DERIVATIVES AND THEIR USE AS MEDICAMENTS

(57) Abstract

The invention relates to triazolo[4,5-*d*]pyrimidin-3-yl derivatives of formula (I), which are useful in the treatment of platelet aggregation disorders.



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TRIAZOLO [4.5-*D*] PYRIMIDINYL DERIVATIVES AND THEIR USE AS MEDICAMENTS

The present invention provides new triazolo[4,5-*d*]pyrimidine compounds, their use as medicaments, compositions containing them and processes for their preparation.

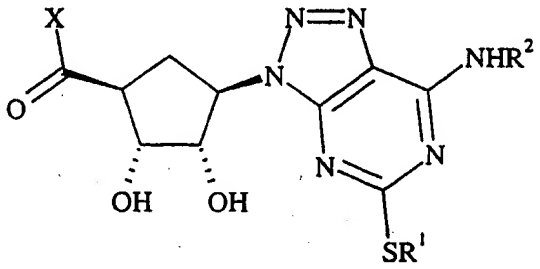
Platelet adhesion and aggregation are initiating events in arterial thrombosis. Although the process of platelet adhesion to the sub-endothelial surface may have an important role to play in the repair of damaged vessel walls, the platelet aggregation that this initiates can precipitate acute thrombotic occlusion of vital vascular beds, leading to events with high morbidity such as myocardial infarction and unstable angina. The success of interventions used to prevent or alleviate these conditions, such as thrombolysis and angioplasty is also compromised by platelet mediated occlusion or re-occlusion.

A number of converging pathways lead to platelet aggregation. Whatever the initial stimulus, the final common event is a cross linking of platelets by binding of fibrinogen to a membrane binding site, glycoprotein IIb/IIIa (GPIIb/IIIa). The high anti-platelet efficacy of antibodies or antagonists for GPIIb/IIIa is explained by their interference with this final common event. However, this efficacy may also explain the bleeding problems that have been observed with this class of agent. Thrombin can produce platelet aggregation largely independently of other pathways but substantial quantities of thrombin are unlikely to be present without prior activation of platelets by other mechanisms. Thrombin inhibitors such as hirudin are highly effective anti-thrombotic agents, but again may produce excessive bleeding because they function as both anti-platelet and anti-coagulant agents (The TIMI 9a Investigators (1994), *Circulation* **90**, pp. 1624-1630; The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIa Investigators (1994) *Circulation* **90**, pp. 1631-1637; Neuhaus K.L. et. al. (1994) *Circulation* **90**, pp.1638-1642).

It has been found that ADP acts as a key mediator of thrombosis. A pivotal role for ADP is supported by the fact that other agents, such as adrenaline and 5-hydroxytryptamine (5HT, serotonin) will only produce aggregation in the presence of ADP. The limited anti-thrombotic efficacy of aspirin may reflect the fact that it blocks only one source of ADP which is that released in a thromboxane-dependent manner following platelet adhesion (see e.g. Antiplatelet Trialists' Collaboration (1994), *Br. Med. J.* **308**, pp. 81-106; Antiplatelet Trialists' Collaboration (1994), *Br. Med. J.* **308**, pp.159-168). Aspirin has no effect on aggregation produced by other sources of ADP, such as damaged cells or ADP released

under conditions of turbulent blood flow. ADP-induced platelet aggregation is mediated by the P_{2T}-receptor subtype uniquely located on the platelet membrane. Recently it has been shown that antagonists at this receptor offer significant improvements over other anti-thrombotic agents. Accordingly there is a need to find P_{2T}-antagonists as anti-thrombotic agents.

It has now been found that a series of triazolo[4,5-*d*]pyrimidine derivatives are P_{2T}-receptor antagonists. In a first aspect the invention therefore provides a compound of formula (I):



(I)

wherein;

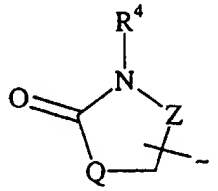
X is OH or NHR^3;

R^1 is C_{1-6}-alkyl, C_{3-8}-cycloalkyl or a phenyl group, each group being optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5,C_{1-6}-thioalkyl and/or C_{1-6}-alkyl (itself optionally substituted by one or more halogen atoms);

R^2 is C_{1-8}-alkyl or C_{2-8}-alkenyl each of which is optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl, C_{3-8}-cycloalkyl, aryl and/or C_{1-6}-alkyl groups; or R^2 is a C_{3-8}-cycloalkyl group optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl, phenyl and/or C_{1-6}-alkyl groups; the optional phenyl substituent being further optionally substituted by one or more halogen atoms and/or NO_2, $C(O)R^4$, OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl groups;

R^3 is hydrogen or C_{1-6}-alkyl substituted by one or more hydroxy and/or phenyl groups and optionally by one or more halogen atoms, wherein the phenyl group is substituted by one or more hydroxy groups and optionally substituted by one or more halogen atoms and/or NO_2, $C(O)R^4$, OR^4, NR^4R^5,C_{1-6}-thioalkyl and/or C_{1-6}-alkyl groups, or R^3 is a C_{1-6}-alkyl group substituted by a $C(O)NR^4R^5$ or a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, wherein

the alkyl group is optionally substituted by one or more hydroxy and/or phenyl groups and wherein the phenyl group is optionally substituted as defined above for R^3; or
R^3 is a lactam ring of formula (i):



wherein Q is a $(CH_2)_m$ moiety wherein m is 1, 2 or 3, Z is O, C(O) or CH_2;
R^4 and R^5 each independently represent hydrogen, phenyl or a C_{1-6}-alkyl wherein the alkyl group is optionally substituted by one or more phenyl groups;
or a salt thereof.

Alkyl groups, whether alone or as part of another group, can be straight chained or branched.

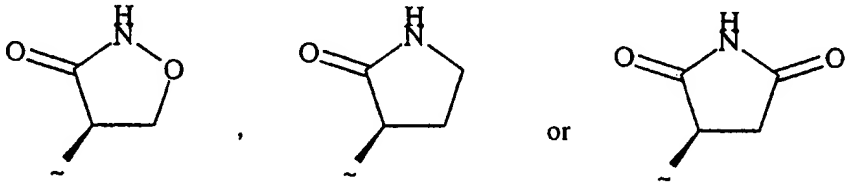
Suitably R^1 is C_{1-6}-alkyl, C_{3-8}-cycloalkyl or a phenyl group, each group being optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl (itself optionally substituted by one or more halogen atoms). Preferably R^1 is C_{1-4}-alkyl, C_{4-8}-cycloalkyl or a phenyl group optionally substituted by one or more halogen atoms or by a CF_3 group. More preferably R^1 is propyl, cyclohexyl or phenyl optionally substituted by two chlorine atoms or by a CF_3 group. Most preferably R^1 is propyl or phenyl substituted in the 4-position by CF_3.

Suitably R^2 is C_{1-8}-alkyl or C_{2-8}-alkenyl each of which is optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl, C_{3-8}-cycloalkyl, aryl and/or C_{1-6}-alkyl groups; or R^2 is a C_{3-8}-cycloalkyl group optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl, phenyl and/or C_{1-6}-alkyl groups; the optional phenyl substituent being further optionally substituted by one or more halogen atoms and/or NO_2, $C(O)R^4$, OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl groups. By the term 'aryl' is meant phenyl and naphthyl. Preferably R^2 is C_{1-6}-alkyl optionally substituted by phenyl or C_{1-6}-thioalkyl or R^2 is a C_{3-8}-cycloalkyl group optionally substituted by phenyl. Most preferably R^2 is butyl or 2-phenylcyclopropyl.

Suitably X is OH or NHR^3 where R^3 is hydrogen or C_{1-6}-alkyl substituted by one or more hydroxy and/or phenyl groups and optionally by one or more halogen atoms, wherein the

phenyl group is substituted by one or more hydroxy groups and optionally substituted by one or more halogen atoms and/or NO_2, $C(O)R^4$, OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl groups, or R^3 is a C_{1-6}-alkyl group substituted by a $C(O)NR^4R^5$ or a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, wherein the alkyl group is optionally substituted by one or more hydroxy and/or phenyl groups and wherein the phenyl group is optionally substituted as defined above, or R^3 is a lactam ring of formula (i).

Preferably R^3 is hydrogen or C_{1-6}-alkyl substituted by hydroxy and optionally by $C(O)NH_2$ or di-fluoro; C_{1-6}-alkyl substituted by $C(O)NH_2$; C_{1-6}-alkyl substituted by C(O)NHMe; C_{1-6}-alkyl substituted by hydroxyphenyl and optionally by $C(O)NR^4R^5$ or R^3 is a lactam ring of formula:

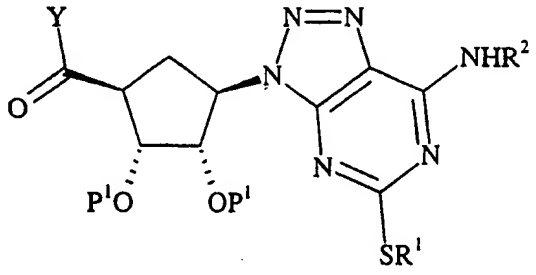


Most preferably R^3 is hydrogen.

Particularly preferred compounds of the invention include those exemplified herein, both in free base form and as pharmaceutically acceptable salts thereof.

According to the invention there is further provided a process for the preparation of a compound of formula (I) which comprises

(a) deprotecting a compound of formula (II):



(II)

wherein R^1 and R^2 are as defined above, P^1 is a protecting group and Y is X as defined above or O-C_{1-6}-alkyl, O-benzyl or NHR^7 wherein R^7 is a C_{1-6}-alkyl group substituted by a $C(O)OR^8$ group and optionally one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, wherein R^4 and R^5 are as defined above and R^8 is C_{1-6}-alkyl (for example methyl, ethyl, isopropyl or t-butyl) or benzyl; and, optionally

(b) reacting the compound of formula (I) thus obtained with a suitable acid or base to prepare a pharmaceutically acceptable salt.

The invention further provides an intermediate of formula (II) wherein its substituents are as defined above. Examples of suitable groups which each P^1 may independently represent are a C_{1-6}-alkyl (preferably methyl), benzyl, $(C_{1-6}\text{-alkyl})_3Si$ (preferably trimethylsilyl) and a $C(O)C_{1-6}$-alkyl group (preferably acetyl). Preferably the two groups P^1 together with the atoms to which they are attached complete a ring, for example the two groups P^1 together represent an alkylidene such as methylidene or, more preferably, isopropylidene, or an alkoxy methylidene such as ethoxymethylidene.

The deprotection reaction in step (a) of the process of the invention may be carried out using methods generally known in the art. Step (a) is preferably carried out as follows:

(i) where one or both of P^1 represent $C(O)C_{1-6}$-alkyl, where Y is O-C_{1-6}-alkyl and/or where Y is NHR^7 and R^8 is C_{1-6}-alkyl, $C(O)C_{1-6}$-alkyl or C_{1-6}-alkyl groups can be removed by basic hydrolysis, for example by using a metal hydroxide, preferably an alkali metal hydroxide, such as sodium hydroxide or lithium hydroxide, or quaternary ammonium hydroxide in a solvent, such as aqueous ethanol or aqueous tetrahydrofuran, at a temperature of from 10° to 100°C, preferably the temperature is around room temperature; or by acidic hydrolysis using a mineral acid such as HCl or a strong organic acid such as trichloroacetic acid in a solvent such as aqueous 1,4-dioxane;

(ii) where one or both of P^1 represent $(C_{1-6}\text{-alkyl})_3Si$, they may be removed by the use of, for example, a fluoride ion source, for example tetra-n-butylammonium fluoride or hydrogen fluoride;

(iii) where one or both of P^1 represent a C_{1-6}-alkyl group, where Y is O-C_{1-6}-alkyl and/or where Y is NHR^7 and R^8 is C_{1-6}-alkyl, C_{1-6}-alkyl groups may be removed by the use of, for example, boron tribromide;

(iv) where Y is O-benzyl, where one or both of P^1 represent a benzyl group and/or where Y is NHR^7 and R^8 is benzyl, benzyl groups may be removed by hydrogenolysis using a transition metal catalyst, for example palladium on charcoal, under an atmosphere of hydrogen, at a pressure of from 1 to 5 bar, in a solvent, such as acetic acid; and/or

(v) where both P^1 together represent alkylidene or an alkoxy alkylidene, they may be removed by the use of, for example, a mineral or organic acid, preferably by using trifluoroacetic acid in dichloromethane or water at room temperature.

Deprotecting a compound of formula (II) as defined above but wherein Y is NHR^7 wherein R^7 is as defined above prepares a compound of formula (I) wherein X is NHR^3 wherein R^3 is a C_{1-6}-alkyl group substituted by a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups. Such deprotection is preferably carried out using a compound of formula (II) as defined above but wherein R^8 is t-butyl and both P^1 together represent isopropylidene with trifluoroacetic acid in dichloromethane at room temperature.

Salts of the compounds of formula (I) may be formed by reacting the free acid, or a salt thereof, or the free base, or a salt or a derivative thereof, with one or more equivalents of the appropriate base (for example ammonium hydroxide optionally substitued by C_{1-6}-alkyl or an alkali metal or alkaline earth metal hydroxide) or acid (for example a hydrohalic (especially HCl), sulphuric, oxalic or phosphoric acid). The reaction may be carried out in a solvent or medium in which the salt is insoluble or in a solvent in which the salt is soluble, e.g. water, ethanol, THF or diethyl ether, which may be removed *in vacuo*, or by freeze drying. The reaction may also be a metathetical process or it may be carried out on an ion exchange resin. The non-toxic physiologically acceptable salts are preferred, although other salts may be useful, e.g. in isolating or purifying the product.

To prepare a compound of formula (II) wherein Y is NHR^3 and R^1, R^2 and P^1 are as defined above , a compound of formula (II) wherein Y is OH and R^1, R^2 and P^1 are as defined above is reacted with R^3NH_2 wherein R^3 is as defined above. The reaction is preferably carried out in the presence of a coupling agent using methods known from

peptide synthesis (see M. Bodanszky and A. Bodanszky, The Practice of Peptide Synthesis, Springer-Verlag, 1984). Suitable coupling agents include 1,1'-carbonyldiimidazole and dicyclohexylcarbodiimide; the preferred coupling agent is bromo-tris-pyrrolidino-phosphonium hexafluorophosphate or benzotriazole-1-yl-oxy-tris-(dimethylamino)phosphoniumhexafluorophosphate, used in the presence of *N,N*-diethylisopropylamine. The reaction is preferably carried out in *N,N*-dimethylformamide (DMF) or tetrahydrofuran (THF) and preferably at a temperature of from -15° to 120°C, more preferably at a temperature of from 0°C to room temperature. This reaction may correspondingly be used to convert a compound of formula (I) wherein X is OH and R^1 and R^2 are as defined above to a compound of formula (I) wherein X is NHR^3 and R^1, R^2 and R^3 are as defined above.

To prepare a compound of formula (II) as defined above but where Y is NHR^7 wherein R^7 is as defined above, a compound of formula (II) wherein Y is OH is reacted with a compound of formula R^7NH_2 wherein R^7 is as defined above, using the coupling conditions described above.

A compound of formula (II) as defined above but wherein Y is NHR^3 wherein R^3 is a C_{1-6}-alkyl group substituted by a $C(O)NR^4R^5$ group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, may be prepared by reacting a compound of formula (II) as defined above but wherein Y is NHR^3 wherein R^3 is a C_{1-6}-alkyl group substituted by a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, with HNR^4R^5 wherein R^4 and R^5 are as defined above in the presence of a coupling agent as defined above. This reaction may also be used to convert a compound of formula (I) as defined above but wherein X is NHR^3 wherein R^3 is a C_{1-6}-alkyl group substituted by a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups to a compound of formula (I) as defined above but wherein X is NHR^3 wherein R^3 is a C_{1-6}-alkyl group substituted by a $C(O)NR^4R^5$ group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups.

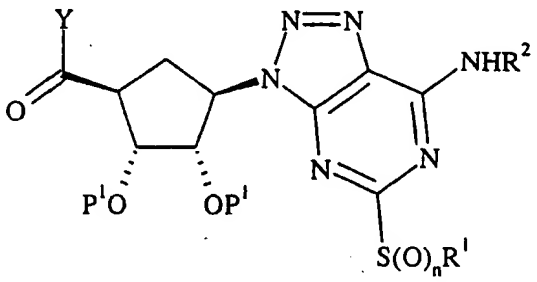
A compound of formula (II) as defined above but wherein Y is NHR^3 wherein R^3 is a C_{1-6}-alkyl group substituted by a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups wherein

R^4 and R^5 are as defined above, may be prepared by deprotecting a compound of formula (II) as defined above but wherein Y is NHR^7 using the deprotection procedures given in (i), (iii) or (iv) above.

A compound of formula (II) wherein Y is NHR^3 or NHR^7 can be prepared by first activating a compound of formula (II) wherein Y is OH and then treating it with R^3NH_2 or R^7NH_2 wherein R^3 and R^7 as defined above, or a salt thereof. The treatment is generally carried out in an inert solvent at a temperature of from -20 to 150°C.

Methods of activating a compound of formula (II) wherein Y is OH include formation of an acyl halide or an acetic anhydride. Acid anhydrides may be formed by treatment with an acyl halide, such as acetyl chloride in the presence of a base, such as pyridine or by treatment with a dehydrating agent such as acetic acid anhydride or phosphorus pentoxide in an inert solvent. Acyl halides may be formed by treatment of the acid with a halogenating agent, for example P(III), P(V) or S(IV) halides such as phosphorus trichloride. Acyl halides may also be prepared by an exchange reaction of the acid with an acyl halide such as oxalyl bromide. The reactions may be performed in the halogenating agent or acyl halide as solvent or in other inert solvents such as methylene chloride, at a temperature of from 0 to 150°C. Activation is preferably carried out by treatment with oxalyl chloride in dichloromethane at room temperature.

The substituent R^1 in the compound of formula (II) may optionally be replaced by first oxidising the compound of formula (II) to a compound of formula III:



(III)

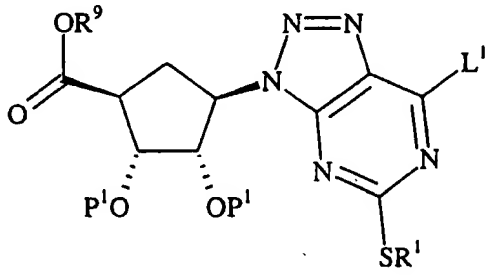
wherein R^1, P^1, Y and R^2 are as defined above and n is 1 or 2, using an organic oxidant such as dimethyldioxirane or an inorganic oxidant such as sodium hypochlorite in an inert solvent, such as dichloromethane or a mixture of methanol and water, at a temperature of from -20 to 40°C, preferably the oxidant is either Oxone (registered trademark) and the reaction is carried out in acetonitrile/water at room temperature or the oxidant is 3-

chloroperoxybenzoic acid and the reaction is carried out in dichloromethane. This reaction may correspondingly be used to change the substituent R^1 in a compound of formula (I).

The compound of formula (III) is then treated with a compound of formula R^1SM wherein R^1 is as defined above and M is an alkali metal, for example lithium or potassium, to give a compound of formula (II) with a different substituent R^1. The reaction is generally carried out in an inert solvent at a temperature of from -20 to 40°C. M is preferably sodium and the reaction is preferably carried out in tetrahydrofuran at room temperature.

A compound of formula R^1SM may be prepared by reacting R^1SH with a base such as C_{1-6}-alkyl-M or MH, wherein M is as defined above, in an inert solvent at a temperature of from -20 to 40°C.

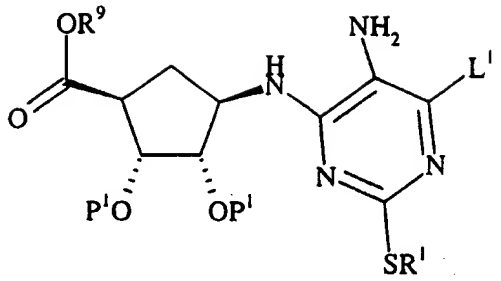
A compound of formula (II) wherein Y is OH, O-C_{1-6}-alkyl or O-benzyl can be prepared by reacting a compound of formula IV:



(IV)

wherein R^1 and P^1 are as defined above, L^1 is a leaving group, for example a halogen atom and R^9 is a H atom or a C_{1-6}-alkyl or benzyl group, with NH_2R^2 or a salt of NH_2R^2 wherein R^2 is as defined above, in the presence of a base. Suitable salts of NH_2R^2 include hydrochlorides. Suitable bases include an organic base such as triethylamine or an inorganic base such as potassium carbonate.

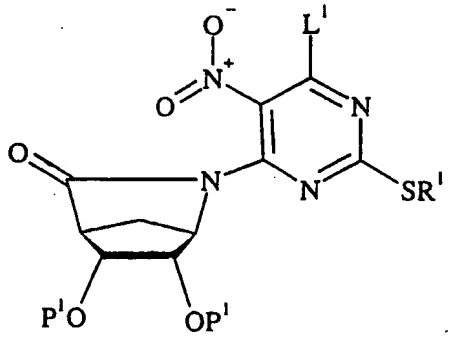
A compound of formula (IV) can be prepared by diazotising a compound of formula V:



(V)

wherein R^1, R^9, L^1 and P^1 are as defined above, with a metal nitrite, for example an alkali metal nitrite, especially sodium nitrite in dilute aqueous acid, for example 2M HCl, or with a C_{1-6}-alkyl nitrite in an inert solvent, at a temperature of from -20 to 100°C; preferred conditions are isoamyl nitrite in acetonitrile at 80°C.

A compound of formula (V) wherein R^9 is H can be prepared by reducing and hydrolysing a compound of formula VI:



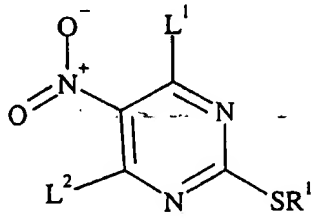
(VI)

wherein R^1, L^1 and P^1 are as defined above. The reduction may be carried for example by using hydrogenation with a transition metal catalyst at a temperature around room temperature, for example palladium on charcoal under an atmosphere of hydrogen, preferably at a pressure from 1 to 5 atmospheres, in a solvent, for example ethanol, or by using iron in an acidic solvent such as acetic acid at a temperature of about 100°C.

To prepare a compound of formula (V) wherein R^9 is H, hydrolysis of the compound of formula (VI) may be performed by using a mineral acid such as HCl or a strong organic acid such as trifluoroacetic acid in a solvent such as aqueous 1,4-dioxane, at a temperature of from 20 to 150°C. Preferably the reduction and hydrolysis are carried out simultaneously using iron in an acidic solvent, for example acetic acid, containing an alkaline earth metal halide, for example calcium chloride, at a temperature of about 80°C.

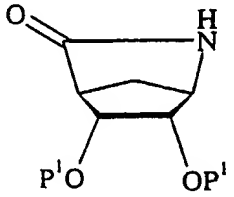
To prepare a compound of formula (V) wherein R^9 is C_{1-6}-alkyl or benzyl, the compound of formula (VI) is treated with iron in acetic acid at a temperature of from 50 to 80°C so that the nitro group is reduced. The resulting intermediate is then treated with sodium borohydride in a mixture of water and C_{1-6}-alkyl alcohol or benzyl alcohol at around room termperature.

A compound of formula (VI) can be prepared by reacting a compound of formula VII:



(VII)

wherein L^1 and R^1 are as defined above and L^2 is a leaving group, for example a halogen atom, wherein L^1 and L^2 are preferably the same, with a compound of formula VIII:



(VIII)

wherein P^1 is as defined above, in the presence of a base such as C_{1-6}-alkyl-M or MH wherein M is as defined above, for example butyl lithium, in an inert solvent, such as tetrahydrofuran (THF), at a temperature of from -10 to 100°C. Preferably sodium hydride is used in THF at room temperature.

A compound of formula (VII) may be prepared from 4,6-dihydroxy-2-mercaptopyrimidine by alkylation with R^1L^3 wherein R^1 is as defined above and L^3 is a suitable leaving group, for example a halogen atom, followed by nitration, whereafter the two alcohols are converted to leaving groups L^1 and L^2.

All novel intermediates form an aspect of the invention. In particular the invention further provides an intermediate of formula (III) wherein R^1, R^2, P^1, n and Y are as defined above.

The compounds of the invention act as P_{2T}-receptor antagonists. Accordingly, the compounds are useful in therapy, especially adjunctive therapy, particularly they are indicated for use as: inhibitors of platelet activation, aggregation and degranulation, anti-thrombotic agents or in the treatment or prophylaxis of unstable angina, coronary angioplasty (PTCA), myocardial infarction, perithrombolysis, primary arterial thrombotic complications of atherosclerosis such as thrombotic or embolic stroke, peripheral vascular disease, myocardial infarction with or without thrombolysis, arterial complications due to interventions in atherosclerotic disease such as angioplasty, endarterectomy, stent placement, coronary and other vascular graft surgery, thrombotic complications of surgical or mechanical damage such as tissue salvage following accidental or surgical trauma, reconstructive surgery including skin and muscle flaps, conditions with a diffuse thrombotic/platelet consumption component such as disseminated intravascular coagulation, thrombotic thrombocytopaenic purpura, haemolytic uraemic syndrome, thrombotic complications of septicaemia, adult respiratory distress syndrome, anti-phospholipid syndrome, heparin-induced thrombocytopaenia and pre-eclampsia/eclampsia, or venous thrombosis such as deep vein thrombosis, venoocclusive disease, haematological conditions such as myeloproliferative disease, including thrombocythaemia; or in the prevention of mechanically-induced platelet activation *in vivo*, such as cardio-pulmonary bypass (prevention of microthromboembolism), mechanically-induced platelet activation *in vitro*, such as use in the preservation of blood products, e.g. platelet concentrates, or shunt occlusion such as in renal dialysis and plasmapheresis, thrombosis secondary to vascular damage/inflammation such as vasculitis, arteritis, glomerulonephritis, inflammatory bowel disease and organ graft rejection, conditions such as migraine, Raynaud's phenomenon, atheromatous plaque formation/progression, vascular stenosis/restenosis and asthma, in which platelet-derived factors are implicated in the disease process.

According to the invention there is further provided the use of a compound according to the invention in the manufacture of a medicament for the treatment of the above disorders, in particular a platelet aggregation disorder. The invention also provides a method for the treatment of the above disorders, in particular a platelet aggregation disorder which comprises administering to a patient suffering from such a disorder a therapeutically effective amount of a compound according to the invention.

The compounds may be administered topically, e.g. to the lung and/or the airways, in the form of solutions, suspensions, HFA aerosols and dry powder formulations; or

systemically, e.g. by oral administration in the form of tablets, pills, capsules, syrups, powders or granules, or by parenteral administration in the form of sterile parenteral solutions or suspensions, or by rectal administration in the form of suppositories or transdermally.

The compounds of the invention may be administered on their own or as a pharmaceutical composition comprising the compound of the invention in combination with a pharmaceutically acceptable diluent, adjuvant or carrier.

Dry powder formulations and pressurized HFA aerosols of the compounds of the invention may be administered by oral or nasal inhalation. For inhalation the compound is desireably finely divided. The finely divided compound preferably has a mass median diameter of less than 10 μm, and may be suspended in a propellant mixture with the assistance of a dispersant, such as a C_8-C_{20} fatty acid or salt thereof, (e.g. oleic acid), a bile salt, a phospholipid, an alkyl saccharide, a perfluorinated or polyethoxylated surfactant, or other pharmaceutically acceptable dispersant.

The compounds of the invention may also be administered by means of a dry powder inhaler. The inhaler may be a single or a multi dose inhaler, and may be a breath actuated dry powder inhaler.

One possibility is to mix the finely divided compound with a carrier substance, e.g. a mono-, di- or polysaccharide, a sugar alcohol or another polyol. Suitable carriers are sugars, e.g. lactose, glucose, raffinose, melezitose, lactitol, maltitol, trehalose, sucrose, mannitol; and starch. Alternatively the finely divided compound may be coated by another substance. The powder mixture may also be dispensed into hard gelatine capsules, each containing the desired dose of the active compound.

Another possibility is to process the finely divided powder into spheres which break up during the inhalation procedure. This spheronized powder may be filled into the drug reservoir of a multidose inhaler, e.g. that known as the Turbuhaler® in which a dosing unit meters the desired dose which is then inhaled by the patient. With this system the active compound with or without a carrier substance is delivered to the patient.

The pharmaceutical composition comprising the compound of the invention may conveniently be tablets, pills, capsules, syrups, powders or granules for oral administration;

sterile parenteral solutions or suspensions for parenteral administration or suppositories for rectal administration.

For oral administration the active compound may be admixed with an adjuvant or a carrier, e.g. lactose, saccharose, sorbitol, mannitol, starches such as potato starch, corn starch or amylopectin, cellulose derivatives, a binder such as gelatine or polyvinylpyrrolidone, and a lubricant such as magnesium stearate, calcium stearate, polyethylene glycol, waxes, paraffin, and the like, and then compressed into tablets. If coated tablets are required, the cores, prepared as described above, may be coated with a concentrated sugar solution which may contain e.g. gum arabic, gelatine, talcum, titanium dioxide, and the like. Alternatively, the tablet may be coated with a suitable polymer dissolved in a readily volatile organic solvent.

For the preparation of soft gelatine capsules, the compound may be admixed with e.g. a vegetable oil or polyethylene glycol. Hard gelatine capsules may contain granules of the compound using either the above mentioned excipients for tablets, e.g. lactose, saccharose, sorbitol , mannitol, starches, cellulose derivatives or gelatine. Also liquid or semisolid formulations of the drug may be filled into hard gelatine capsules.

Liquid preparations for oral application may be in the form of syrups or suspensions, for example solutions containing the compound, the balance being sugar and a mixture of ethanol, water, glycerol and propylene glycol. Optionally such liquid preparations may contain colouring agents, flavouring agents, saccharine and carboxymethylcellulose as a thickening agent or other excipients known to those skilled in art.

The invention is illustrated by the following examples which should not be interpreted as limiting the invention. In the examples the NMR spectra were measured on a Varian Unity Inova 300 spectrometer and the MS spectra were measured as follows: EI spectra were obtained on a VG 70-250S or Finnigan Mat Incos-XL spectrometer, FAB spectra were obtained on a VG70-250SEQ spectrometer, ESI and APCI spectra were obtained on Finnigan Mat SSQ7000 or a Micromass Platform spectrometer. Preparative HPLC separations were generally performed using a Novapak®, Bondapak® or Hypersil® column packed with BDSC-18 reverse phase silica. Flash chromatography (indicated in the Examples as (SiO_2)) was carried out using Fisher Matrix silica, 35-70 μm.

Example 1

[1*S*-(1α,2β,3β,4α)]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

(a) 4,6-Dihydroxy-2-(propylthio)pyrimidine

Propyl iodide (136ml) was added to a suspension of 4,6-dihydroxy-2-mercaptopyrimidine (200g) in water (800ml), containing sodium hydroxide (55.6g). The reaction mixture was stirred for 2 weeks then concentrated to half volume, 2N hydrochloric acid was added and the subtitle compound was isolated by filtration (167g).

MS (EI) 186 (M^+, 100%).

(b) 4,6-Dihydroxy-5-nitro-2-(propylthio)pyrimidine

The product of step (a) (70g) was added slowly to ice-cooled fuming nitric acid (323ml). The reaction mixture was stirred for 1 hour then poured onto ice and the subtitle compound was isolated by filtration (65g).

MS (EI) 231 (M^+), 41 (100%).

(c) 4,6-Dichloro-5-nitro-2-(propylthio)pyrimidine

N,N-Diethylaniline (150ml) was added dropwise to a stirred suspension of the product of step (b) (134g) in phosphoryl chloride (500ml) then the resulting solution heated at reflux for 1 hour. The cooled reaction mixture was poured onto ice then extracted with diethyl ether (3x500ml). The combined extracts were dried and concentrated. Chromatography (SiO_2, isohexane: diethyl ether, 19:1 as eluant) gave the subtitle compound (128g).

MS (EI) 271, 269, 267 (M^+), 41 (100%).

(d) [3a*S*-(3aα,4β,7β,7aα)] 5-[6-Chloro-5-nitro-2-(propylthio)pyrimidin-4-yl]-tetrahydro-2,2-dimethyl-4,7-methano-1,3-dioxolo[4,5-*c*]pyridin-6(3a*H*)-one

Sodium hydride (60%, 4.00g) was added portionwise to [3a*S*-(3aα,4β,7β,7aα] tetrahydro-2,2-dimethyl-4,7-methano-1,3-dioxolo[4,5-*c*]pyridin-6(3a*H*)-one (18.3g) in THF (500ml). On stirring for 1 hour the solution was added dropwise to the product of step (c) (54.0g) in THF (500ml). The reaction mixture was stirred at room temperature for 45 minutes then concentrated and purified by chromatography (SiO_2, dichloromethane : isohexane, 3:2 as eluant) to afford the subtitle compound (79.2g).

MS (APCI) 417, 415 ($M+H^+$), 415 (100%).

(e) [3a*R*-(3aα,4α,6α,6aα)]-6-[[5-Amino-6-chloro-2-(propylthio)-4-pyrimidinyl]amino]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Iron powder (10.0g) was added to a stirred solution of the product of step (d) (10.0g), and calcium chloride (1.49g) in ethanol (140ml). The reaction mixture was heated at reflux for 10 minutes then filtered through celite, washing several times with hot ethanol. The filtrate was concentrated to afford the subtitle compound (9.3g).

MS (FAB) 405, 403 ($M+H^+$), 405 (100%).

(f) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-Chloro-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Isoamyl nitrite (6.02ml) was added to a solution of the product of step (e) (9.28g) in acetonitrile (80ml) and the solution heated at 70°C for 1 hour. The cooled reaction mixture was concentrated and purified (SiO_2, ethyl acetate:isohexane 2:1 as eluant) to afford the subtitle compound (7.9g).

MS (FAB) 416, 414 ($M+H^+$), 414 (100%).

(g) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

The product from step (f) (5.52g) and butylamine (5ml) in 1,4-dioxane (25ml) were stirred at room temperature for 1 hour. The reaction mixture was concentrated and the residue purified (SiO_2, dichloromethane:ethyl acetate 2:1 as eluant) to afford the subtitle compound (2.2g).

MS (FAB) 451 ($M+H^+$, 100%).

(h) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide

Oxalyl chloride (0.24ml) was added dropwise to a solution of the product of step (g) (0.60g) in dichloromethane (15ml) and the solution stirred at room temperature for 2 hours then concentrated. The residue was taken into dichloromethane (10ml) cooled to 0°C and 880 ammonia (10ml) added, then the solution stirred at room temperature for 18 hours. The resulting solid was collected by filtration and dried under vacuum to afford the subtitle compound (0.48g).

MS (FAB) 438 ($M+H^+$, 100%).

(i) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxycyclopentanecarboxamide

A solution of the product from step (h) (0.48g) in trifluoroacetic acid (9ml)/water (1ml) was stirred at room temperature for 5 hours. The reaction mixture was concentrated and the residue purified by chromatography (SiO_2, dichloromethane:methanol, 15:1 as eluant) to afford the title compound (0.17g).

Melting point: 209-211°C (EtOAc)

NMR δH (d_6-DMSO) 8.96 (1H, t), 7.40-6.90 (2H, m), 5.03-4.96 (2H, m), 4.22 (1H, m), 3.89 (1H, m), 3.40 (2H, m), 2.80 (2H, m), 2.43-2.31 (2H, m), 1.73-1.51 (4H, m), 1.37-1.31 (2H, m), 0.98 (3H, t), 0.90 (3H, t).

Example 2

[1*S*-(1α,2β,3β,4α)]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of Example 1 step (i) using the product of Example 1 step (g).

NMR δH (d_6-DMSO) 9.01-8.98 (1H, t), 5.03-4.96 (1H, m), 4.42-4.39 (1H, m), 4.21 (1H, m), 3.89 (1H, m), 3.52-3.46 (2H, m), 3.15-3.03 (2H, m), 1.73-1.55 (4H, m), 1.37-1.31 (2H, m), 0.98 (3H, t), 0.91 (3H, t).

MS (FAB) 411 ($M+H^+$, 100%).

Example 3

[1*S*-(1α,2β,3β,4α)]-4-[7-(cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

(a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of Example 1 step (g) using the product of Example 1 step (f) and cyclopropylamine.

NMR δH (d_6-DMSO) 7.95 (1H, d), 5.72 (1H, m), 5.58 (1H, m), 5.12 (1H, d), 3.36-3.01 (2H, m), 3.02-2.88 (2H, m), 2.60-2.46 (1H, m), 1.88-1.78 (2H, m), 1.56 (3H, s), 1.45 (3H, s), 1.10 (3H, t), 0.75 (2H, t), 0.38 (2H, br s).

(b) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazol[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of Example 1 step (h) using the product of step (a).

MS (FAB) 434 ($M+H^+$, 100%).

(c) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of Example 1 step (i) using the product of step (b).

MS (FAB) 394 ($M+H^+$, 100%).

Example 4

[1*S*-(1α,2β,3β,4α)]-4-[7-(cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of Example 1 step (i) using the product of Example 3 step (a).

MS (APCI) 395 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.10 (1H, d), 5.07 (1H, m), 4.45 (1H, m), 4.42 (1H, m), 3.26-3.00 (3H, m), 2.80 (1H, t), 2.57-2.43 (2H, m), 1.74 (2H, m), 1.01 (3H, t), 0.94-0.72 (4H, m).

Example 5

[1*S*-[1α,2β,3β,4α(trans)]]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

(a) [3a*R*-[3aα,4α,6α(trans),6aα]]-6-[7-[2-Phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of Example 1 step (g) using the product of Example 1 step (f), *(trans)* 2-phenylcyclopropylamine hydrochloride and triethylamine.

MS (APCI) 511 ($M+H^+$, 100%).

(b) [1*S*-(1α,2β,3β,4α)]-4-[(2-Phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of Example 1 step (i) using the product of step (a).

MS (APCI) 471 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.36 (1H, d), 7.31-7.15 (5H, m), 5.01 (1H, q), 4.40 (1H, m), 4.21 (1H, m), 3.19 (1H, m), 2.91-2.82 (3H, m), 2.51-2.13 (4H, m), 1.53-1.48 (2H, m), 1.34 (1H, m), 0.81 (2H, m).

Example 6

[1*S*-[1α,2β,3β,4α(trans)]]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)-amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 5 and purified by flash chromatography (SiO_2, chloroform:methanol 93:7 as eluant).

MS (APCI) 470 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.36 (1H, d), 7.39 (1H, s), 7.29 (2H, m), 7.18 (3H, m), 6.93 (1H, s), 5.12 (1H, d), 4.99 (1H, d), 4.96 (1H, m), 4.39 (1H, m), 4.11 (1H, q), 3.20 (1H, m), 2.89 (2H, m), 2.74 (1H, m), 2.28 (2H, m), 2.13 (1H, m), 1.47 (3H, m), 1.34 (1H, m), 0.81 (3H, t).

Example 7

[1*S*-(1α,2β,3β,4α)]]-2,3-dihydroxy-4-[7-(2-phenylethylamino)-5-(propylthio)-*3H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

(a) [3a*S*-(3aα,4β,7β,7aα)] 5-[5-amino-6-chloro-2-(propylthio)-pyrimidin-4-yl]-tetrahydro-2,2-dimethyl-4,7-methano-1,3-dioxolo[4,5-*c*]pyridin-6(3a*H*)-one

Reduced iron powder (50g) was added to a solution of the product of Example 1 step (d) (50.0g) in glacial acetic acid (1800ml) and the reaction mixture heated at reflux for 15 minutes. The cooled reaction mixture was concentrated and the residue taken into ether (300ml) then washed with sodium bicarbonate solution (2x200ml). The organic phase was dried and concentrated and the residue purified (SiO_2, dichloromethane:diethyl ether 9:1 as eluant) to afford the subtitle compound (42.6g).

(b) [3a*R*-(3aα,4α,6α,6aα)]-6-[[5-Amino-6-chloro-2-(propylthio)-4-pyrimidinyl]amino]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid, methyl ester

Sodium borohydride (0.60g) was added, over 30 minutes to an ice-cooled solution of the product of step (a) (4.50g) in methanol (100ml). The solution was concentrated and purified by chromatography (SiO_2, dichloromethane : ethyl acetate, 95:5 as eluant) to give the subtitle compound (2.1g).

MS (APCI) 419, 417 ($M+H^+$), 417 (100%).

Further elution gave [3a*R*-(3aα,4α,6α,6aα)]-6-[[5-amino-6-chloro-2-(propylthio)-4-pyrimidinyl]amino]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-methanol (2.4g).

MS (APCI) 419, 417 ($M+H^+$), 417 (100%).

(c) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-Chloro-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid, methyl ester

Prepared according to the method of Example 1 step (f) using the product of step (b).

MS (FAB) 430, 428 ($M+H^+$), 417 (100%).

(d) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(2-Phenylethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid, methyl ester

Prepared according to the method of Example 1 step (g) using the product of step (c), phenylethylamine hydrochloride and potassium carbonate.

MS (APCI) 513 ($M+H^+$, 100%).

(e) [1*S*-(1α,2β,3β,4α)]-4-[7-(2-Phenylethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid, methyl ester

Prepared according to the method of Example 1 step (i) using the product of step (d).

MS (APCI) 473 ($M+H^+$, 100%).

(f) [1*S*-(1α,2β,3β,4α)]-4-[7-(2-Phenylethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxycyclopentanecarboxylic acid

Lithium hydroxide monohydrate (56mg) was added to a solution of the product of step (e) (0.25g) in THF (30ml) / water (30ml). The solution was stirred at room temperature for 18 hours then 2M HCl (aq) added until the pH was 7 before extracting with ethyl acetate (3x40ml). The combined organics were dried and concentrated to afford the title compound.

MS (APCI) 459 ($M+H^+$, 100%)

Elemental analysis Found C: 54.77; H: 5.72; N: 18.00; S: 7.34%
Required C: 55.00; H: 5.72; N: 18.30; S: 7.00%

Example 8

[1*S*-(1α,2β,3β,4α)]-2,3-dihydroxy-4-[7-(2-phenylethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 7.

NMR δH (d_6-DMSO) 9.10 (1H, d), 7.31 (1H, s), 7.30-7.15 (4H, m), 6.94 (1H, s), 5.14 (1H, d), 5.00 (1H, d), 5.00-4.90 (1H, m), 4.45-4.30 (1H, m), 4.20-4.00 (1H, m), 3.80-3.60 (2H,

m), 3.20-3.00 (2H, m), 3.00-2.90 (2H, m), 2.80-2.70 (1H, m), 2.40-2.10 (2H, m), 1.75-1.60 (2H, m), 0.97 (3H, t).

Example 9

[1*S*-(1α,2β,3β,4α)]-2,3-dihydroxy-4-[7-[2-(methylthio)ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

The product of Example 1 step (f) (2.0g) and 2-(methylthio)ethylamine (0.91g) in 1,4-dioxane (25ml) were stirred at room temperature for 1 hour. The reaction mixture was concentrated and the residue taken into trifluoroacetic acid (20ml)/water (10ml) then stirred at room temperature for 1 hour. The reaction mixture was concentrated and the residue purified by chromatography (HPLC, Nova-pak ® C18 column, 0.1% ammonium acetate:methanol, 60:40 as eluant) to afford the product (0.17g).

MS (APCI) 429 ($M+H^+$, 100%).
NMR δH (d_6-DMSO) 5.00 (1H, m), 4.44 (1H, m), 4.19 (1H, m), 3.71 (2H, m), 3.01 (2H, m), 2.78-2.65 (3H, m), 2.35 (2H, t), 2.12 (3H, s), 1.74 (2H, m), 0.98 (3H, m).

Example 10

[1*S*-(1α,2β,3β,4α)]-2,3-dihydroxy-4-[7-[2-(methylthio)ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 9.

MS (APCI) 428 ($M+H^+$, 100%).
NMR δH (d_6-DMSO) 9.07 (1H, t), 8.66 (1H, t), 7.38 (1H, s), 6.93 (1H, s), 5.15 (2H, br s), 4.97 (1H, m), 4.46 (1H, m), 4.12 (1H, m), 3.70 (2H, m), 3.10 (2H, m), 2.75 (3H, m), 2.39-2.18 (2H, m), 1.70 (2H, m), 1.00 (3H, t).

Example 11

[1*S*-[1α,2β,3β,4α(trans)]]-4-[5-(Cyclohexylthio)-7-[2-(phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

(a) **[3a*R*-[3aα,4α,6α,6aα(trans)]]-Tetrahydro-2,2-dimethyl-6-[7-(2-phenylcyclopropylamino)-5-(propylsulfonyl)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

3-Chloroperoxybenzoic acid (0.14g) was added to a solution of the product of Example 5 step (a) (0.11g) in dichloromethane (8ml) and the resulting solution stirred at room temperature for 18 hours. The solution was washed with aqueous sodium metabisulfite solution (3 x 10ml) then dried and concentrated. Purification by chromatography (SiO_2, ethyl acetate: isohexane, 1:1 as eluant) gave the subtitle compound (0.12g).

MS (APCI) 543 ($M+H^+$, 100%).

(b) **[3a*R*-[3aα,4α,6α,6aα(trans)]]-6-[5-(cyclohexylthio)-7-[2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Cyclohexanethiol (0.16g) was added dropwise to a suspension of sodium hydride (60%, 55mg) in *N,N*-dimethylformamide (DMF) (10ml). After 30 minutes, a solution of the product of step (a) (0.30g) in DMF (10ml) was added dropwise over 45 minutes then the reaction was stirred for 45 minutes. The reaction mixture was added slowly to a solution of sodium chloride (10ml), containing acetic acid (1ml) then the solution extracted with ethyl acetate (50ml). The organic phase was dried and concentrated and the residue purified by chromatography (SiO_2, ethyl acetate: isohexane, 2:1 as eluant) to give the subtitle compound (0.26g).

MS (APCI) 551 ($M+H^+$, 100%).

(c) **[1*S*-[1α,2β,3β,4α(trans)]]-4-[5-(Cyclohexylthio)-7-[2-(phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

Prepared according to the method of Example 1 step (i) using the product of step (b).

MS (APCI) 511 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 12.42 (1H, s), 7.29 (2H, m), 7.18 (3H, m), 5.16 (2H, m), 5.00 (1H, q), 4.42 (1H, m), 4.22 (1H, q), 3.58 (1H, m), 3.20 (1H, m), 2.82 (1H, m), 2.40 (2H, m), 2.15 (1H, m), 1.94 (1H, m), 1.79 (1H, m), 1.57-1.18 (10H, m).

Example 12

[1*S*-[1α,2β,3β,4α(trans)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(cyclohexylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 11.

MS (APCI) 510 ($M+H^+$, 100%).
NMR δH (d_6-DMSO) 9.32 (1H, d), 7.37 (1H, s), 7.29 (2H, m), 7.18 (3H, m), 6.92 (1H, s), 5.11 (1H, d), 4.93 (2H, m), 4.40 (1H, q), 4.12 (1H, m), 3.60 (1H, m), 3.20 (1H, m), 2.75 (1H, m), 2.28 (2H, m), 2.14 (1H, m), 1.92 (1H, m), 1.77 (1H, m), 1.57-1.18 (10H, m).

Example 13

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

(a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-(propylsulfonyl)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**
Prepared according to the method of Example 11 step (a) using the product of Example 1 step (g).

MS (APCI) 483 ($M+H^+$), 349 (100%).

(b) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylsulfonyl)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**
Prepared according to the method of Example 1 step (i) using the product of step (a).

MS (APCI) 443 ($M+H^+$, 100%).

(c) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

Prepared according to the method of Example 11 step (b) using the product of step (b) and 3,4-dichlorothiophenol.

MS (APCI) 517, 515, 513 ($M+H^+$), 513 (100%).
NMR δH (d_6-DMSO) 12.40 (1H, br s), 9.15 (1H, t), 7.94 (1H, s), 7.72 (1H, d), 7.61 (1H, d), 4.97-4.94 (1H, m), 4.36-4.33 (1H, m), 4.19-4.16 (1H, m), 3.21-3.14 (2H, m), 2.82-2.78 (1H, m), 2.51-2.44 (1H, m), 2.26-2.21 (1H, m), 1.33 (2H, q), 1.13 (2H, q), 0.79 (3H, t).

Example 14

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 13.

MS (APCI) 516, 514, 512 ($M+H^+$), 512 (100%).
NMR δH (d_6-DMSO) 9.16 (1H, t), 7.95-7.60 (3H, m), 7.40 (1H, s), 6.92 (1H, s), 5.14 (1H, d), 4.99 (1H, d), 4.92-4.89 (1H, m), 4.36-4.34 (1H, m), 4.08-4.05 (1H, m), 3.20-3.14 (2H, m), 2.76-2.72 (1H, m), 2.49-2.18 (2H, m), 1.35-1.30 (2H, m), 1.16-1.09 (2H, m), 0.79 (3H, t).

Example 15

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of Example 11 step (b) using the product of Example 13 step (b) and 4-(trifluoromethyl)thiophenol.

MS (APCI) 513 ($M+H^+$,100%).
NMR δH (d_6-DMSO) 9.14 (1H, t), 7.88 (2H, d), 7.81 (2H, d), 5.00-4.91 (1H, m), 4.35-4.33 (1H, m), 4.16-4.10 (1H, m), 3.16-3.14 (2H, m), 2.78-2.75 (1H, m), 2.41-2.21 (2H, m), 1.36-1.27 (2H, q), 1.15-1.03 (2H, q), 0.77 (3H, t).

Example 16

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 15.

MS (APCI) 512 ($M+H^+$,100%).

NMR δH (d_6-DMSO) 9.14 (1H, t), 7.90-7.79 (4H, m), 7.39 (1H, br s), 6.95 (1H, br s), 5.14 (1H, d), 4.99 (1H, d), 4.93 (1H, m), 4.36-4.34 (1H, m), 4.06 (1H, m), 3.15 (2H, q), 2.76-2.72 (1H, m), 2.49-2.19 (2H, m), 1.33-1.29 (2H, m), 1.12-1.05 (2H, m), 0.76 (3H, t).

Example 17

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(phenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of Example 11 step (b) using the product of Example 13 step (b) and thiophenol.

MS (APCI) 445 ($M+H^+$,100%).

NMR δH (d_6-DMSO) 9.01 (1H, t), 7.62 (2H, m), 7.46-7.43 (3H, m), 4.95-4.86 (1H, q), 4.36-4.31 (1H, m), 4.16-4.09 (1H, m), 3.20-3.14 (2H, m), 2.72-2.68 (1H, m), 2.50-2.17 (2H, m), 1.39-1.29 (2H, m), 1.19-1.07 (2H, m), 0.79 (3H, t),

Example 18

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(phenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (h) using the product of Example 17.

MS (APCI) 444 ($M+H^+$,100%).
NMR δH (d_6-DMSO) 9.03 (1H, t), 7.64-7.44 (5H, m), 7.39 (1H, s), 6.95 (1H, m), 5.12 (1H, m), 4.99 (1H, m), 4.89 (1H, m), 4.35-4.31 (1H, m), 4.07 (1H, m), 3.17-3.15 (2H, m), 2.75-2.72 (1H, m), 2.49-2.16 (2H, m), 1.35-1.34 (2H, m), 1.12 (2H, m), 0.79 (3H, t).

Example 19

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo*4,5*-d*]*pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

(a) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-(propylsulfonyl)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**
Prepared according to the method of Example 11 step (a) using the product of Example 3.

MS (APCI) 426 ($M+H^+$,100%).

(b) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**
Prepared according to the method of Example 11 step (b) using the product of step (a) and 3, 4-dichloro-thiophenol.

MS (APCI) 498, 496 ($M+H^+$), 496 (100%).
NMR δH (d_6-DMSO) 9.28 (1H, d), 8.01 (1H, d), 7.81-7.60 (2H, m), 7.40 (1H, s), 6.95 (1H, s), 5.11 (1H, d), 4.98 (1H, d), 4.85 (1H, d), 4.35 (1H, m), 4.07 (1H, q), 2.80 (2H, m), 2.31 (1H, m), 2.11 (1H, m), 0.65 (4H, m).

Example 20

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide

(a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-Chloro-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]-pyrimidin-3-yl]-*N*-(2-hydroxyethyl)-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**
N,N-Diisopropylethylamine (0.52ml) was added to a solution of ethanolamine (66ml), bromo-tris-pyrrolidino-phosphonium hexafluorophosphate (0.56g) and the product of Example 1 step (g) (0.45g) in DMF (15ml). The reaction mixture was stirred at room temperature for 1 hour then concentrated. Chromatography (SiO_2, ethyl acetate as eluant) gave the subtitle compound (0.18g).

MS (APCI) 494 ($M+H^+$, 100%).

(b) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (i) using the product of step (a) (55mg).

MS (APCI) 454 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.00 (1H, t), 7.94 (1H, t), 5.13 (1H, d), 5.00-4.93 (2H, m), 4.68 (1H, t), 4.45-4.11 (1H, m), 4.10 (1H, m), 3.53-3.38 (4H, m), 3.17-3.07 (4H, m), 2.78 (1H, m), 2.33-2.24 (2H, m), 1.74-1.57 (4H, m), 1.38-1.30 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 21

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]yrimidin-3-yl]-2,3-dihydroxy-*N*-(3-hydroxy-2,2-difluoropropyl)-cyclopentanecarboxamide

(a) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-*N*-(3-hydroxy-2,2-difluoropropyl)-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide

Prepared according to the method of Example 20 step (a) using 2,2-difluoro-1,3-propanediamine and was isolated as a by-product.

MS (APCI) 544 ($M+H^+$, 100%).

(b) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(3-hydroxy-2,2-difluoropropyl)cyclopentane-carboxamide

Prepared according to the method of Example 1 step (i) using the product of step (a).

MS (APCI) 504 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.00 (1H, t), 8.32 (1H, t), 8.46 (1H, t), 5.18 (1H, d), 5.04 (1H, d), 5.01-4.92 (1H, m), 4.48-4.39 (1H, m), 4.14-4.10 (1H, m), 3.64-3.48 (6H, m), 3.12-3.06 (2H, m), 2.93-2.83 (1H, m), 2.37-2.10 (3H, m), 1.73-1.57 (4H, m), 1.36-1.30 (2H, m), 0.98 (3H, t), 0.90 (3H, t).

Example 22

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(4-hydroxyphenyl)ethyl]-cyclopentanecarboxamide

(a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-*N*-[2-(4-hydroxyphenyl)ethyl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of Example 20 step (a) using (4-hydroxyphenyl)ethylamine.

MS (APCI) 570 ($M+H^+$, 100%).

(b) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(4-hydroxyphenyl)ethyl]-cyclopentanecarboxamide**

Prepared according to the method of Example 1 step (i) using the product of step (a).

MS (APCI) 530 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.16 (1H, br s), 8.98 (1H, m), 7.97 (1H, m), 6.99 (2H, d), 6.67 (2H, d), 5.12 (1H, d), 4.97-4.93 (2H, m), 4.42 (1H, m), 4.10 (1H, m), 3.48 (2H, m), 3.26-3.19 (2H, m), 3.13-3.07 (2H, m), 2.78-2.70 (1H, m), 2.60 (2H, t), 2.31-2.24 (2H, m), 1.74-1.58 (4H, m), 1.38-1.31 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 23

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide

(a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-(propylsulfonyl)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Oxone® (5.0g) was added to a solution of the product of Example 1 step (f) (1.0g) in acetonitrile (150ml)/ water (10ml) and the resulting solution was stirred at room temperature for 3 hours. The solution was then diluted with water (100ml) and extracted with ethyl acetate (3 x 75ml). The combined extracts were dried and concentrated and the

residue purified (SiO_2, ethyl acetate: methanol, 9:1 as eluant) to give the subtitle compound (0.79g).

MS (ESI) 467 ($M+H^+$, 100%).

(b) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of Example 11 step (b) using the product of step (a) and 4-(trifluoromethyl)thiophenol (0.38g).

MS (ESI) 553 ($M+H^+$, 100%).

(c) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-*N*-(2-hydroxyethyl)-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide

Prepared according to the method of Example 20 step (a) using the product of step (b).

MS (ESI) 596 ($M+H^+$, 100%).

(d) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide

Prepared according to the method of Example 1 step (i) using the product of step (a).

MS (APCI) 556 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.14 (1H, t), 7.94 (1H, m), 7.89 (1H, m), 5.14 (1H, d), 4.99 (1H, d), 4.93 (1H, m), 4.70 (1H, t), 4.38 (1H, m), 4.06 (1H, m), 3.44 (2H, m), 3.18 (4H, m), 2.78 (1H, m), 2.33 (1H, m), 2.17 (1H, m), 1.33 (2H, m), 1.09 (2H, m), 0.76 (3H, t).

Example 24

[1*S*-(1α,2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

(a) **[1*S*-(1α,2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 20, step (a) using the product of example 1 step (g) and (2S)-2-amino-3-hydroxy-propanamide hydrochloride.

MS (APCI) 537 ($M+H^+$, 100%).

(b) **[1*S*-(1α,2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

A solution of the product of step (a) (0.39g) in methanol (10ml)/0.1N HCl(aq) (20ml) was stirred at room temperature for 2 hours. The solution was concentrated and the residue purified (HPLC, Nova-pak ® C18 column, 0.1% aqueous ammonium acetate:methanol, gradient elution 50:50 to 0:100 over 15 minutes) to afford the subtitle compound.

MS (APCI) 497 ($M+H^+$, 100%).

NMR δH (d_6-DMSO): 9.01 (1H, t), 7.89 (1H, d), 7.28 (2H, d), 5.19 (1H, d), 5.09 (1H, d), 4.97 (1H, m), 4.87 (1H, t), 4.38 (1H, m), 4.27 (1H, m), 4.13 (1H, m), 3.59 (2H, m), 3.50 (2H, m), 3.09 (2H, m), 2.94 (1H, m), 2.34-2.26 (2H, m), (2H, m), 1.72 (2H, s), 1.62 (2H, m), 1.36 (1H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 25

[1*S*-[1α(*S),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-*N*-(tetrahydro-3-oxo-isoxazol-4-yl)-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of Example 20 step (a) using the product of Example 2 and D-cycloserine.

Melting point: 209-211 °C (EtOAc)

MS (APCI) 495 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 11.53 (1H, s), 9.01 (1H, t), 8.55 (1H, d), 5.16 (1H, d), 5.03 (1H, d), 4.98 (1H, q), 4.78 (1H, m), 4.55 (1H, t), 4.42 (1H, q), 4.11 (1H, m), 3.95 (1H, t), 3.49 (2H, q), 3.10 (2H, m), 2.83 (1H, m), 2.39 (1H, m), 2.27 (1H, m), 1.70 (2H, m), 1.60 (2H, m), 1.34 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 26

[1*S*-[1α(*R),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-oxo-pyrrolidin-3-yl)-cyclopentanecarboxamide**

(a) [1*S*-[1α(*R),2β,3β,4α]]-6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-tetrahydro-2,2-dimethyl-*N*-(2-oxo-pyrrolidin-3-yl)-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of Example 20 step (a) using 3-amino-pyrrolidin-2-one hydrochloride (prepared as described in by R. Pellegata, M. Pinza, G. Pifferi, Synthesis 1978, 614).

MS (APCI) 533 ($M+H^+$, 100%).

(b) [1*S*-[1α(*R),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-oxo-pyrrolidin-3-yl)-cyclopentanecarboxamide**

A solution of the product from step (a) (0.44g) in trifluoroacetic acid (25ml)/dichloromethane (25ml) was stirred at room temperature for 5 hours. The reaction mixture was concentrated and the residue purified by chromatography (HPLC, Nova-pak ® C18 column, 0.1% aqueous ammonium acetate:methanol, gradient elution 50:50 to 0:100 over 15 minutes) to afford the title compound (0.16g).

MS (APCI) 493 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.00 (1H, t), 8.25 (1H, d), 7.84 (1H, s), 5.05 (1H, br s), 5.21 (1H, br s), 4.98 (1H, m), 4.53 (1H, m), 4.33 (1H, m), 4.09 (1H, m), 3.47 (2H, m), 3.13 (2H, m), 3.08 (2H, m), 2.81 (1H, m), 2.34 (3H, m), 1.78 (1H, m), 1.74 (2H, m), 1.69 (2H, m), 1.60 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 27

[1*S*-[1α(*R),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2,3-di-oxo-pyrrolidin-3-yl)-cyclopentanecarboxamide**

(a) **[1*S*-[1α(*R**),2β,3β,4α]]-6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2,5-di-oxo-pyrrolidin-3-yl)-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of Example 20 step (a) using 3-amino-2,5-pyrrolidinedione (prepared as described by T Polonski, J. Chem. Soc., 1988, 629).

MS (APCI) 547 ($M+H^+$, 100%).

[1*S*-[1α(*R),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-oxo-pyrrolidin-3-yl)-cyclopentanecarboxamide**

Prepared according to the method of example 26 step (b) using the product of step (a).

MS (APCI) 507 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 11.22 (1H, s), 8.99 (1H, t), 8.63 (1H, d), 5.17 (1H, d), 5.15 (1H, d), 4.99 (1H, m), 4.46 (2H, m), 4.12 (1H, m), 3.49 (2H, m), 3.11 (2H, m), 2.93 (1H, m), 2.77 (1H, m), 2.56 (1H, m), 2.36-2.34 (2H, m), 1.71 (2H, m), 1.64 (2H, m), 1.36 (2H, m), 0.98 (3H, t), 0.91 (3H, t).

Example 28

[1*S*-[1α(*R),2β,3β,4α]]-*N*-[(Aminocarbonyl)-methyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared using the method of Example 20 step (a) using aminoacetamide, followed by the method of Example 26 step (b).

MS (APCI) 467 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.99 (1H, t), 8.08 (1H, d), 7.28 (1H, s), 7.05 (1H, s), 4.98 (1H, m), 4.40 (1H, m), 4.12 (1H, m), 3.66 (2H, m), 3.46 (2H, m), 2.85 (1H, m), 2.38-2.27 (2H, m), 1.74 (2H, m), 1.62 (2H, m), 1.36 (2H, m), 0.99 (3H, t), 0.89 (3H, t).

Example 29

[1*S*-[1α(*R),2β,3β,4α]]-N-[1-(Aminocarbonyl)-2-(4-hydroxyphenyl)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

(a) **[1*S*-[1α(*R**),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(4-hydroxyphenyl)ethyl]-[6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of Example 20 step (a) using (S)-α-amino-4-hydroxy-benzenepropanamide.

MS (APCI) 613 ($M+H^+$, 100%).

(b) **[1*S*-[1α(*R**),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(4-hydroxyphenyl)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of Example 26 step (b) using the product of step (a).

MS (APCI) 573 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.07 (1H, s), 8.98 (1H, t), 8.61 (1H, t), 8.03 (1H, d), 7.39 (1H, s), 7.07 (1H, s), 7.00 (2H, d), 6.58 (2H, d), 4.92 (1H, m), 4.36 (2H, m), 4.10 (1H, m), 3.90 (2H, m), 3.50 (2H, m), 3.09 (2H, m), 2.86 (2H, m), 2.66 (1H, m), 2.21 (1H, m), 2.06 (1H, m), 1.71 (2H, m), 1.61 (2H, m), 1.36 (2H, m), 0. 99 (3H, t), 0. 91 (3H, t)..

Example 30

[1*S*-[1α(*R),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-4-[7-(butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

(a) **[3a*R*-[3aα,4α,6α,6aα]]-6-[7-(butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid (0.38g)**

Prepared according to the method of Example 11 (b) using the product of example 23, step (a) and 4-(trifluoromethyl)thiophenol.

MS (ESI) 553 ($M+H^+$, 100%).

(b) [1*S*-[1α(*R),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-4-[7-(butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of Example 20 step (a), followed by the method of Example 26 step (b) using the product of step (a) above.

MS (ESI) 599 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.73 (1H, s), 7.80 (4H, d), 7.56 (1H, d), 6.89 (2H, br s), 4.94 (1H, m), 4.81 (1H, d), 4.72 (1H, d), 4.71 (1H, t), 4.42 (1H, m), 4.31 (1H, m), 4.20 (1H, m), 3.69 (2H, m), 3.61 (2H, m), 2.99 (1H, m), 2.51-2.25 (2H, m), 1.43 (2H, br s), 1.21 (2H, br s), 0.84 (3H, t).

Example 31

[1*S*-[1α(1*R,2*S**),2β,3β,4α]]-*N*-[1-(Amino-carbonyl)-2-(hydroxy)propyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxycyclopentanecarboxamide**

(a) [1*S*-[1α(1*R,2*S**),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)propyl]-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of Example 20 step (a) using [*S*-(*S**,*S**)]-2-amino-3-hydroxy-butanamide.

MS (APCI) 551 ($M+H^+$, 100%).

(b) [1*S*-[1α(1*R,2*S**),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)propyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of Example 26 step (b) using the product of step (a) and purified by chromatography (HPLC, Nova-pak.® C18 column, 0.1% aqueous ammonium acetate:methanol, gradient elution 30:70 to 0:100 over 15 minutes).

MS (APCI) 511 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.98 (1H, t), 7.68 (1H, d), 7.15 (2H, d), 5.18 (1H, d), 5.08 (1H, d), 4.97(1H, m), 4.84 (1H, d), 4.40-4.38 (1H, m), 4.17 (1H, d), 4.14 (1H, d), 4.05 (1H, br s),

3.49 (2H, q), 3.12-3.08 (2H, m), 3.06-3.00 (1H, m), 2.40 (1H, m), 2.26 (1H, m), 1.69 (2H, m), 1.63 (2H, m), 1.34 (2H, m), 1.02 (3H, sext), 0.99 (3H, t), 0. 91 (3H, t).

Example 32

[1*S*-[1α,2β,3β,4α]]-N-[2-(Aminocarbonyl)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

(a) [3a*R*-[3aα,4α,6α,6aα]]-*N*-[2-(Aminocarbonyl)ethyl]-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide

Prepared according to the method of example 20 step (a) using 3-amino-propanamide.

MS (APCI) 521 ($M+H^+$, 100%).

(b) [1*S*-[1α,2β,3β,4α]]-*N*-[2-(Aminocarbonyl)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of Example 26 step (b) using the product of step (a) above.

MS (APCI) 481 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.99 (1H, t), 7.97 (1H, t), 7.33 (1H, br s), 6.84 (1H, br s), 5.05 (1H, br s), 4.97-4.92 (1H, m), 4.43-4.39 (1H, m), 4.09 (1H, m), 3.52-3.46 (2H, m), 3.28-3.22 (2H, m), 3.12-3.07 (2H, m), 2.75-2.72 (1H, m), 2.31-2.20 (4H, m), 1.73-1.55 (4H, m), 1.37-1.31 (2H, m), 1.01-0.88 (6H, m).

Example 33

[1*S*-[1α,2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(methylaminocarbonyl)-ethyl]-cyclopentanecarboxamide

(a) [3a*R*-[3aα,4α,6α,6aα]]-*N*-[6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carbonyl]-β-alanine, 1,1-dimethylethyl ester

Prepared according to the method of Example 20 step (a) using β-alanine, 1,1-dimethylethyl ester.

MS (APCI) 578 ($M+H^+$, 100%).

(b) [1*S*-[1α,2β,3β,4α]]-*N*-[4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxycyclopentyl-4-carbonyl]-β-alanine

Prepared according to the method of Example 26 step (b) using the product of step (a) above.

MS (APCI) 482 ($M+H^+$, 100%).

(c) [1*S*-[1α,2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(Methylaminocarbonyl)ethyl]-cyclopentane-carboxamide

Prepared according to the method of example 20 step (a) using the product of step (b) and methylamine.

MS (APCI) 495 ($M+H^+$, 100%).
NMR δH (d_6-DMSO) 9.01 (1H, t), 8.00-7.98 (1H, m), 7.81 (1H, m), 5.13 (1H, d), 5.01 (1H, d), 4.96-4.92 (1H, m), 4.44-4.40 (1H, m), 4.12-4.08 (1H, m), 3.48 (2H, q), 3.26 (2H, q), 3.13-3.07 (2H, m), 2.76-2.74(1H, m), 2.55 (3H, d), 2.31-2.21 (4H, m), 1.70 (2H, sext), 1.62 (2H, m), 1.34 (2H, sext), 0.99 (3H, t), 0. 91 (3H, t).

Example 34

[1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid**

a) [3a*R*-[3aα,4α,6α(1*R,2*S**),6aα]]-Tetrahydro-2,2-dimethyl-6-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

A mixture of the product of example 1, step f) (413 mg), (1*R-trans*)-2-phenylcyclopropylamine, [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1) (prepared as described by L.A. Mitscher et al., J. Med. Chem. 1986, **29**, 2044) (283 mg) and triethylamine (1.1 ml) in dichloromethane (6 ml) was stirred at room temperature for 4 hours. The reaction mixture was concentrated and the residue purified (SiO_2, ethyl acetate then methanol:ethyl acetate 1:4 as eluant) to afford the subtitle compound (390 mg).

MS (APCI) 511 ($M+H^+$, 100%).

b) [1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 471 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.34 and 8.98 (1H, d), 7.31-7.15 (5H, m), 5.18 (2H, br s), 5.02 (1H, m), 4.42 (1H, m), 4.22 (1H, m), 3.22 (1H, m), 3.17-2.75 (3H, m), 2.50-2.08 (3H, m), 1.78-1.25 (4H, m), 0.81 and 0.99 (3H, t).

Example 35

[1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

a) [3a*R*-[3aα,4α,6α(1*R,2*S**),6aα]]-Tetrahydro-2,2-dimethyl-6-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 1, step h) using the product of example 34, step a).

MS (APCI) 510 ($M+H^+$, 100%).

b) [1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[7-(2-phenylcyclopropylamino)]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 470 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.32 and 8.92 (1H, d), 7.34 (1H, m), 7.29 (2H, m), 7.18 (3H, m), 6.89 (1H, s), 5.09 (1H, d), 4.97 (2H, m), 4.42 (1H, m), 4.14 (1H, m), 3.21 and 3.88 (1H, m), 2.96 (1H, m), 1.51 and 1.70 (1H, m), 1.32 (1H, m), 0.82 and 1.00 (3H, t)

Example 36
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-(cyclobutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Cyclobutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 1, step g) using the product of example 1, step f) and cyclobutylamine.

MS (APCI) 449 ($M+H^+$, 100%).

b) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclobutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 409 ($M+H^+$, 100%).
NMR δH (d_6-DMSO) 0.95-1.01(3H, m), 1.64-1.90 (4H, m), 2.11-2.45 (6H, m), 2.75-2.82 (1H, m), 3.03-3.14 (2H, m), 4.19-4.22 (1H, m), 4.38-4.45 (1H, m), 4.61-4.69 (1H, m), 4.95-5.03 (1H, m), 9.22 (1H, d)

Example 37
[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclobutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Sieber amide resin (2.0g) was washed sequentially with a 20% solution of piperidine in *N,N*-dimethylformamide (10 ml), *N,N*-dimethylformamide (DMF) (3 x10 ml), dichloromethane (3 x10 ml) and diethyl ether (1 x10 ml). To the resin was added a solution of the product from example 36 step b) (0.25g) in dichloromethane (10ml) and *N,N'*-diisopropylcarbodiimide (0.13g). The mixture was shaken for 18 hours then filtered and the residue washed with dichloromethane and a solution of trifluoroacetic acid in dichloromethane (2%, 4 x10 ml). The filtrate was evaporated to dryness and the residue purified by chromatography (HPLC, Nova-pak® C18 column, 0.1% aqueous ammonium

acetate:methanol, gradient elution 40:60 to 0:100 over 20 minutes) to afford the title compound (0.095g).

MS (APCI) 408 ($M+H^+$, 100%)

NMR δH (d_6-DMSO) 0.96-1.02 (3H, m), 1.64-1.76 (4H, m), 2.08-2.39 (6H, m), 2.72-2.80 (1H, m), 3.05-3.15 (1H, m), 4.61-4.69 (1H, m), 4.91-4.99 (2H, m), 5.11 (1H, d), 6.91 (1H,s), 7.36 (1H, s), 9.23(1H, d)

Example 38

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-[[4-(trifluoromethyl)phenyl]thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid.

Prepared according to the method of example 11, step b) using the product of example 19, step a) and 4-(trifluoromethyl)thiophenol, followed by the method of example 1 step i).

MS (EI) 497 ($M+H^+$)

NMR δH (d_6-DMSO) 9.32-9.22 (2H, d), 7.95-7.92 (2H , d), 7.81-7.78 (2H, d), 4.98-4.86 (1H, m) 4.40-4.34 (1H, m), 4.18-4.10 (1H, m), 2.76-2.66 (2H, m), 2.5-2.1(2H, t), 0.89-0.50 (4H, m).

Example 39

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-[[4-(trifluoromethyl)phenyl]thio]-3*H* -1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide.

Prepared according to the method of example 1, step h) using the product of example 38, followed by the method of example 1, step i).

MS (EI) 496 ($M+H^+$)

NMR δH (d_6-DMSO) 9.25 (1H, d), 7.95-7.92 (2H, d),7.81-7.78 (2H, d), 7.37 (1H, s) 6.94 (1H, s), 5.15 (1H, d), 4.96 (1H, d), 4.98-4.86 (1H, m), 4.40-4.34 (1H, m), 4.13-4.02 (1H, m), 2.76-2.66 (2H, m), 2.51-2.10 (2H, t), 0.89-0.50 (4H, m).

Example 40

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α,6aα)]-6-[[5-Amino-6-chloro-2-[(3,3,3-trifluoropropyl)thio]-4-pyrimidinyl]amino]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step e), using 4,6-dichloro-5-nitro-2-(3,3,3-trifluoropropylthio)pyrimidine (Prepared as described in WO 9703084).

b) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-Chloro-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step f) using the product of step a).

MS (EI, negative ionization) 466 ($M-H^+$).

c) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step g) using the product of step b) and butylamine.
MS (APCI) 505 ($M+H^+$, 100%).

d) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid.

Prepared according to the method of example1, step i) using the product of step c).
MS (APCI) 465 ($M+H^+$)

NMR δH (d_6-DMSO) 9.10 (1H, t), 4.97-4.93 (1H, m), 4.45 (1H, br s), 4.2 (1H, br s), 3.55-3.50 (2H, m), 3.33-3.22 (1H, m), 2.80-2.55 (2H, m), 2.35-2.33 (2H, m), 1.71 (2H, s), 1.65-1.52 (2H, m),1.4-1.3 (2H, m), 0.90 (1H t).

Example 41

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of example 1, step h) using the product of example 40, step c), followed by the method of example 1, step i).
MS (EI) 464 ($M+H^+$)

NMR δH (d_6-DMSO) 9.10 (1H, t), 7.4 (1H s), 6.93 (1H s), 5.1 (1H, d), 5.00-4.93 (2H, m), 4.12-4.00 (1H, m), 3.56-3.46 (3H, m), 3.35-3.25 (2H, t), 2.82-2.60 (3H, m), 2.4 -2.15 (2H, m), 1.7-1.5 (2H m), 1.4-1.3 (2H m) 0.92-0.88 (3H t).

Example 42

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and 1,4-dimethylpentylamine.

MS (APCI) 493 ($M+H^+$, 100%).

b) [1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 493 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.83-0.86 (6H, m), 0.97-1.00 (3H, t), 1.20-1.25 (4H, m), 1.51-1.54 (2H, m), 1.67-1.72 (3H, m), 2.33-2.40 (2H, m), 2.72-2.76 (1H, m), 3.06-3.10 (2H, m), 4.20-4.46 (3H, m), 4.95-5.01 (2H, m), 8.73 (1H, d)

Example 43

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo*[4,5-d]*pyrimidin-3-yl]-cyclopentanecarboxamide

a) **[3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 20, step a) using the product of example 42, step a) and a solution of ammonia in acetonitrile.

MS (APCI) 479 ($M+H^+$, 100%).

b) **[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 452 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.82-0.86 (6H, m), 0.98 (3H, t), 1.18-1.25 (5H, m), 1.49-1.72 (5H, m), 2.24-2.34 (2H, m), 2.75-2.76 (1H, m), 3.06-3.10 (2H, m), 4.11-4.14 (2H, m), 4.93-5.00 (2H, m), 5.13 (1H, d), 6.92 (1H, s), 7.38 (1H, s), 8.82 (1H, d)

Example 44

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) **[3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 1, step g) using the product of example 1, step f) and 1-methylbutylamine.

NMR δH (d_6-DMSO) 0.81-0.90 (5H, m), 1.03-1.11 (7H, m), 1.21-1.44 (8H, m), 1.55 (3H, s), 1.75-1.80 (3H, m), 2.50-2.59 (1H, m), 2.77-2.84 (2H, m), 2.99-3.06 (2H, m), 3.14-3.23 (2H, m), 4.07-4.18 (1H, m), 5.12-5.14 (1H, m), 5.64-5.66 (2H, m), 7.76 (1H, d)

b) 1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]yrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 425 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.84-0.90 (3H, m), 0.98 (3H, t), 1.19-1.35 (5H, m), 1.48-1.52 (2H, m), 1.62-1.73 (4H, m), 2.35-2.46 (2H, m), 2.76-2.80 (1H, m), 3.04-3.10 (2H, m), 4.20-4.22 (1H, m), 4.39-4.43 (2H, m), 4.97-5.03 (1H, m), 8.79 (1H, d)

Example 45

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

a) [3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide

Prepared according to the method of example 20, step a) using the product of example 44, step a) and a solution of ammonia in acetonitrile.

MS (APCI) 479 ($M+H^+$, 100%).

b) [1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 452 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.82-0.86 (6H, m), 0.98 (3H, t), 1.18-1.25 (5H, m), 1.49-1.72 (5H, m), 2.24-2.34 (2H, m), 2.75-2.76 (1H, m), 3.06-3.10 (2H, m), 4.11-4.14 (2H, m), 4.93-5.00 (2H, m), 5.13 (1H, d), 6.92 (1H, s), 7.38 (1H, s), 8.82 (1H, d)

Example 46

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,3-dimethylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(1,3-dimethylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and 1,3-dimethylbutylamine.

MS (APCI) 479 ($M+H^+$, 100%).

b) [1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,3-dimethylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 439 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.83-0.91 (6H, m), 0.95-1.00 (3H, t), 1.18-1.33 (4H, m), 1.58-1.73 (4H, m), 2.30-2.40 (3H, m), 2.67-2.72 (1H, m), 3.02-3.10 (2H, m), 4.17-4.20 (1H, m), 4.38-4.48 (2H, m), 4.94-5.00 (1H, m), 8.78(1H, d)

Example 47

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,3-dimethylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of example 1, step h) using the product from example 46, step b).

MS (APCI) 438 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.83-0.91 (6H, m), 0.98 (3H, t), 1.18-1.34 (4H, m), 1.58-1.74 (4H, m), 2.20-2.36 (2H, m), 2.72-2.76 (1H, m), 3.06-3.11 (2H, m), 4.10-4.14 (1H, m), 4.39-4.49 (2H, m), 4.93-4.98 (2H, m), 5.11 (1H, d), 6.91 (1H, s), 7.37 (1H, s), 8.79 (1H, d)

Example 48

[1*S*-(1α,2β,3β,4α)]-4-[7-(Ethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and ethylamine, followed by the method of example 1, step i).

MS (APCI) 381(M-H^+).

NMR δH (d_6-DMSO) 8.98 (1H, t), 5.04-4.99 (1H, m), 4.43-4.39 (1H, m), 4.33-4.22 (1H, m), 3.53-3.50 (2H, m), 3.11-3.05 (2H, m), 2.85-2.75 (1H, m), 2.35-2.25(1H, m), 1.80-1.60 (2H, t),1.30-1.15 (3H, t),1.00-0.92 (3H, t).

Example 49

[1*S*-(1α,2β,3β,4α)]-4-[7-(4-Hydroxybutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-6-[7-(4-hydroxybutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and 4-aminobutanol.

MS (APCI) 467 ($M+H^+$, 100%).

b) [1*S*-(1α,2β,3β,4α)]-4-[7-(4-Hydroxybutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 427 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.00 (1H, t), 5.19 (2H, br s), 5.00 (1H, q), 4.43-4.39 (2H, m), 4.22 (1H, t), 3.49 (2H, q), 3.41(2H, q), 3.13-3.03(2H, m), 2.85-2.78 (1H, m), 2.49-2.31 (2H, m), 1.74-1.59 (4H, m), 1.52-1.45 (2H, m), 0.99 (3H, t).

Example 50

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopentylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and cyclopentylamine, followed by the method of example 1, step i).

MS (APCI) 423 (M+H, 100%).

NMR δH (d_6-DMSO) 9.98 (1H, d), 5.23 (1H, bs), 4.97 (2H, q), 4.37-4.21 (1H, m), 3.22-3.01 (2H, m), 2.83 (1H, m), 2.50-2.20 (1H, m), 2.10-1.90 (2H, m), 1.83-1.51 (8H, m), 0.98 (3H, t).

Example 51

[1S-(1α,2β,3β,4α)]-4-[5-[(4-Bromophenyl)thio]-7-(butylamino)-3*H*-1,2,3-triazolo[4,5-*d*]yrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of example 11, step b) using the product of Example 13, step a) and 4-bromothiophenol.

MS (ESI) 525, 523 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.15-9.11 (1H, t), 7.64-7.55 (4H, 2d), 5.24-5.20 (1H, m), 5.01 (1H, m), 4.36-4.33 (1H, m), 4.19-4.16 (1H, m), 3.24-3.17 (2H, m), 2.92-2.84 (1H, m), 2.26-2.21 (1H, m), 1.38-1.31 (2H, m), 1.19-1.12 (2H, m), 0.87-0.80 (3H, t)

Example 52

[1*S*-(1α,2β,3β,4α)]-4-[7-[(6-Hydroxyhexyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid.

Prepared according to the method of example 1, step g) using the product of example 1, step f) and 6-amino-1-hexanol, followed by the method of example 1, step i).

MS (APCI) 455 ($M+H^+$).

NMR δH (d_6-DMSO) 12.44 (1H, s), 9.00 (1H, s), 5.20-5.15 (2H, m), 5.05-4.95 (1H, m), 4.55-4.3 (2H, m), 4.25-4.2 (1H, m), 3.50-3.40 (2H, m), 3.40-3.30 (2H, m), 3.15-3.05 (1H, t), 2.85-2.75 (1H, t), 2.5-2.35 (1H, m), 1.75-1.6 (2H, m), 1.64-1.52 (2H, m), 2.45-2.25 (1H, m), 1.00 (1H, t).

Example 53

[1*S*-[1α,2β,3β,4α(*trans*)]]-2,3-Dihydroxy-4-[5-[[4-(trifluoromethyl)phenyl]thio]-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α(*trans*),6aα]]-Tetrahydro-2,2-dimethyl-6-[7-[(2-phenylcyclopropyl)amino]-5-(propylsulfonyl)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 11, step a) using the product of example 5, step a).

MS (APCI) 543 ($M+H^+$, 100%).

b) [3a*R*-[3aα,4α,6α(*trans*),6aα]]-Tetrahydro-2,2-dimethyl-6-[5-[[4-(trifluoromethyl)phenyl]thio]-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 11, step b) using the product of step a) and 4-trifluoromethylthiophenol.

MS (APCI) 613 ($M+H^+$, 100%).

c) [1*S*-[1α,2β,3β,4α(*trans*)]]-2,3-Dihydroxy-4-[5-[[4-(trifluoromethyl)phenyl]thio]-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of step b).

MS (APCI) 573 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.44 (1H, d), 7.89-7.59 (4H, m), 7.29-7.06 (5H, m), 5.16 (1H, br s), 4.96 (1H, q), 4.34 (1H,br s), 4.15 (1H, t), 3.12-3.00 (1H, m), 2.84-2.77 (1H, m), 2.46-2.40 (1H, m), 2.30-2.20 (2H, m), 1.42-1.35 (1H, m), 1.18-1.07 (1H, m).

Example 54

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(cyclopentylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

Prepared according to the method of example 11, step b) using the product of example 13, step a) and cyclopentanethiol, followed by the method of example 1, step i.

MS (APCI) 437 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.95 and 8.60 (1H, t), 5.00 (1H, m), 4.41 (1H, m), 4.22 (1H, m), 3.98 (1H, m), 3.48 and 3.89 (2H, q), 3.32 (2H, br, s), 2.81 (1H, td), 2.5-2.3 (2H, m), 2.19 (2H, m), 1.63 (8H, m), 1.34 (2H, sextet). 0.91 (3H, t)

Example 55

[1S-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(3-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α,6aα)]-tetrahydro-2,2-dimethyl-6-[7-[(3-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and (3-methylbutyl)amine.

MS (APCI) 465 ($M+H^+$, 100%)

NMR δH (d_6-DMSO) 7.95 (1H, d), 5.72 (1H, m), 5.58 (1H, m), 5.12 (1H, d), 3.36-3.01 (2H, m), 3.02-2.88 (2H, m), 2.60-2.46 (1H, m), 1.88-1.78 (2H, m), 1.56 (3H, s), 1.45 (3H, s), 1.10 (3H, t), 0.75 (2H, t), 0.38 (2H, br s).

b) (1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(3-Methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product from step a).

MS (APCI) 425 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 12.43 (1H, s), 8.73(1H, t), 5.16-5.19 (2H, m), 5.00 (1H, q), 4.70-4.30 (1H, m), 4.22 (1H, t), 3.49-3.96 (2H, m), 3.06-3.12 (2H, m), 2.79-2.82 (1H, m), 2.46-2.32 (2H, m), 1.62-1.73 (3H, m), 1.48-1.54 (2H, m), 0.99 (3H, t), 0.94 (6H, d).

Example 56

[1*S*-[1α,2β,3β,4α (1*R,2*S**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid**

a) [3a*R*-[3aα,4α,6α(1*S,2*R**),6aα]]-Tetrahydro-2,2-dimethyl-6-[7-[(2-phenylcyclopropyl)amino)]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

A mixture of the product of example 1, step f) (1.0 g), (1*S*-*trans*)-2-phenylcyclopropylamine[*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1) (prepared as described by L.A. Mitscher et al., J. Med. Chem. 1986, **29**, 2044) (680 mg) and diisopropylethylamine (1.68 ml) in dichloromethane (30 ml) was stirred at room temperature for 3 days. The reaction mixture was concentrated and the residue purified (SiO_2, dichloromethane:methanol:acetic acid 1650:150:1 as eluant) to afford the subtitle compound (862 mg).

MS (APCI) 511 ($M+H^+$, 100%).

b) [1*S*-[1α,2β,3β,4α (1*R,2*S**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 471 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 12.42 (1H, br s), 9.34 and 8.98 (1H, d), 7.31-7.15 (5H, m), 5.02 (1H, m), 4.40 (1H, m), 4.22 (1H, m), 3.19 (1H, m), 3.16-2.75 (3H, m), 2.50-2.08 (3H, m), 1.75-1.22 (4H, m), 0.82 and 0.98 (3H, t)

Example 57

[1*S*-[1α(*R),2β,3β,4α]]-*N*-(3-Amino-3-oxo-2-propyl)-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentylcarboxamide.**

a) [3a*R*-[3aα,4α(*S),6α,6aα]]-*N*-(3-Amino-3-oxo-2-propyl)-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 20, step a), using the product of example 1, step g) and (2*S*)-2-amino-propanamide, hydrobromide.

MS (APCI) 521 ($M+H^+$, 100%).

b) [1*S*-[1α(*R),2β,3β,4α]]-*N*-(3-Amino-3-oxo-2-propyl)-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentylcarboxamide.**

Prepared according to the method of example 1, step i) using the product of step a).

NMR δH (d_6-DMSO) 8.99 (1H, t), 8.04 (1H, d), 7.31 (1H, s), 7.03 (1H, s), 4.97 (1H, q), 4.40 (1H, t), 4.25 (1H, m), 4.12 (1H, t), 3.50 (2H, q), 3.09 (2H, m), 2.87 (1H, m), 2.27 (2H, m), 1.69 (2H, m), 1.60 (2H, m), 1.36 (2H, m), 1.19 (2H, d), 0.99 (3H, t), 0.91 (3H, t).

Example 58

[1*S*-[1α(*R),2β,3β,4α]]-3-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-hydroxy-1-(methylamino)-1-oxo-2-propyl]-cyclopentanecarboxamide**

Prepared according to the method of example 20, step a) using the product of example 1, step g) and (2*S*)-2-amino-3-hydroxy-*N*-methyl-propanamide, hydrochloride (prepared as described by Zahn, H. Reinert, G , Hoppe-Seyler, Z-Physiol.Chem, 1968, **349**, 608) followed by the method of example 1, step i).

NMR δH (d_6-DMSO) 8.98 (1H, t), 7.93 (1H, d), 7.80 (1H, d), 5.17 (1H, d), 5.07 (1H, d), 4.97 (1H, m), 4.88 (1H, t), 4.45 (1H, m), 4.28 (1H, m), 4.17 (1H, m), 3.53 (4H, m), 3.10 (2H, m), 2.93 (1H, m), 2.61 (3H, d), 2.24-2.37 (2H, m), 1.73 (2H, m), 1.64 (2H, m), 1.64 (2H, m), 1.35 (2H, m), 0.98 (3H, t), 0.90 (3H, t).

Example 59

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-(dimethylamino)-3-oxo-propyl]-cyclopentanecarboxamide

a) **[3a*R*-(3aα,4α,6α,6aα)]-*N*-[6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxol-4-ylcarbonyl]-β-alanine, 1,1-dimethylethyl ester**

N,N-Diisopropylethylamine (0.37ml) was added to a solution of β-alanine, 1,1-dimethylethyl ester, hydrochloride (0.20g), benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphoniumhexafluorophosphate (0.49g) and the product of example 1, step g) (0.45g) in THF (10ml). The reaction mixture was stirred at room temperature for 3 hours then concentrated. The residue was taken into ethyl acetate and washed with saturated aqueous sodium bicarbonate solution then dried and concentrated. Purification (SiO_2, dichloromethane:methanol 197:3 as eluant) gave the subtitle compound (0.45g).

MS (APCI) 578 ($M+H^+$, 100%).

b) **[1*S*-(1α,2β,3β,4α)] -*N*-[[4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-cyclopent-1-yl]carbonyl]-β-alanine**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 482 ($M+H^+$, 100%).

c) **[1*S*-(1α,2β,3β,4α)] 4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-(dimethylamino)-3-oxo-propyl]-cyclopentanecarboxamide**

Prepared according to the method of step a) using the product of step b) and dimethylamine hydrochloride.

MS (FAB) 509 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.91 (3H, t), 0.99 (3H, t), 1.31-1.37 (2H, m), 1.58-1.73 (4H, m), 2.24-2.31 (2H, m), 2.69-2.73 (2H, m), 2.74-2.76 (1H, m), 2.81 (3H, s), 2.94 (3H, s), 3.07-3.12 (2H, m), 3.25-3.33 (2H, m), 3.47-3.50 (2H, m), 4.08-4.11 (1H, m), 4.40-4.42 (1H, m), 4.93-5.20 (3H, m), 7.93 (1H, t), 8.99 (1H, t).

Example 60

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(dimethylamino)-2-oxo-ethyl)-cyclopentanecarboxamide

a) [3a*R*-(3aα,4α,6α,6aα)]-*N*-[[6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxol-4-yl]carbonyl]-glycine, 1,1-dimethylethyl ester

Prepared according to the method of example 59, step a) using the product of example 1, step g) and glycine, 1,1-dimethylethyl ester, hydrochloride.

MS (APCI) 564 ($M+H^+$, 100%).

b) **[1*S*-(1α,2β,3β,4α)]-*N*-[[4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-cyclopent-1-yl]carbonyl]-glycine**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 468 ($M+H^+$, 100%).

c) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(dimethylamino)-2-oxo-ethyl)-cyclopentanecarboxamide**

Prepared according to the method of example 59, step a) using the product of step b) and dimethylamine hydrochloride.

MS (FAB) 495 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.90 (3H, t), 1.01 (3H, t), 1.30-1.38 (2H, m), 1.57-1.73 (4H, m), 2.23-2.38 (2H, m), 2.83 (3H, s), 2.86-2.92 (1H, m), 2.95 (3H, s), 3.06-3.12 (2H, m), 3.46-3.52 (2H, m), 3.94-3.96 (2H, m), 4.13 (1H, m), 4.95-5.14 (3H, m), 7.98 (1H, t), 8.98 (1H, t).

Example 61

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-oxo-3-[(phenylmethyl)amino]-propyl]-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 59, step b) and benzylamine.

MS (APCI) 571 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.91 (3H, t), 0.99 (3H, t), 1.32-1.37 (2H, m), 1.58-1.73 (4H, m), 2.15-2.34 (4H, m), 2.72-2.78 (1H, m), 3.07-3.12 (2H, m), 3.49-3.50 (2H, m), 4.11-4.12 (1H, m), 4.24-4.28 (2H, m), 4.42-4.44 (1H, m), 4.93-4.98 (2H, m), 5.12-5.14(1H, m), 7.19-7.29 (5H, m), 8.01 (1H, t), 8.39 (1H, t), 8.99 (1H, t).

Example 62

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*] pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(methylamino)-2-oxo-ethyl)-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 60 step b) and methylamine hydrochloride.

MS (APCI) 481 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.88-1.00 (6H, m), 1.30-1.38 (2H, m), 1.57-1.73 (4H, m), 2.26-2.38 (3H, m), 2.59 (2H, d), 2.86-2.87 (1H, m), 3.06-3.12 (2H, m), 3.46-3.52 (2H, m), 3.68 (2H, d), 4.13 (1H, t), 4.38-4.42 (1H, m), 4.94-5.00 (2H, m), 7.75 (2H, d), 8.14 (1H, t), 8.98 (1H, t).

Example 63

[1*S*-(1α(*R),2β,3β,4α)]-*N*-[4-Amino-1-(aminocarbonyl)-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3yl]-2,3-dihydroxy-cyclopentanecarboxamide.**

a)[3a*R*-(3aα,4α(*S),6α,6aα)]-*N*-[4-Amino-1-(aminocarbonyl)-4-oxo-butyl]-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole]-cyclopentanecarboxamide.**

Sieber amide resin (1.0g) was washed sequentially with a solution of piperidine in dimethylformamide (20%; 10 ml), *N,N*-dimethylformamide (DMF) (3x10ml) and dichloromethane (3x10ml). To the resin was added a solution of *N*-α-(9-fluorenylmethoxycarbonyl)-L-glutamine (0.37g) in DMF (10ml) , followed by *N,N'*-diisopropylcarbodiimide (0.16ml) and the mixture stirred for 4 hours. The mixture was filtered and the residue washed sequentially with dichloromethane (3x10ml), DMF (3x10ml), a solution of piperidine in DMF (20%, 10 ml) , DMF (3x10ml) and dichloromethane (3x10ml). The resin was suspended in dichloromethane (5ml) and treated with the product of example 1, step g) (0.30g) and *N,N'*-diisopropylcarbodiimide (0.16ml). After stirring for 16 hours the resin was washed with dichloromethane (3x10ml) then trifluoroacetic acid in dichloromethane (2%, 3x10ml). The combined washings were concentrated and the residue purified by chromatography (HPLC, Nova-pak® C18 column, 0.1% aqueous ammonium acetate:acetonitrile, gradient elution 40:60 to 60:40 over 12 minutes) to afford the subtitle compound (0.05g).

MS (APCI) 578 ($M+H^+$, 100%)

b) [1S-(1α(R*),2β,3β,4α)]-*N*-[4-Amino-1-(aminocarbonyl)-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3yl]-2,3-dihydroxy-cyclopentanecarboxamide.

Prepared according to the method of example 1, step i) using the product of step a).

NMR δH (d_6-DMSO) 9.00 (1H, t), 8.03 (1H, d), 7.34 (1H, s), 7.25 (1H, s), 7.08 (1H, s), 6.73 (1H, s), 4.97 (1H, q), 4.40 (1H, t), 4.14 (1H, t), 3.51 (2H, q), 3.10 (2H, m), 2.91 (1H, m), 2.38 (1H, m), 2.21 (1H, m), 2.06 (2H, t), 1.88 (1H, m), 1.69 (3H, m), 1.60 (2H, m), 1.36 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 64

[1*S*-(1α,2β,3β,4α)]-*N*-[4-Amino-1-[(methylamino)carbonyl]-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

a) (2*S*)-5-Amino-*N*-methyl-2-[[(1,1-dimethylethoxy)carbonyl]amino]-5-oxo-propanamide

Prepared according to the method of example 20, step a) using *N*-2-[(1,1-dimethylethoxy)carbonyl]-L-glutamine and methylamine hydrochloride.

MS (APCI) 258 ($M-H^+$),184 (100%)

b) (4*S*)-4-Amino-5-(methylamino)-5-oxo-pentanamide hydrochloride

A solution of the product from step a) (0.52g) in 4M hydrogen chloride/1,4-dioxane (10ml) was stirred at room temperature for 2 hours. The reaction mixture was concentrated and the residue purified by reverse phase chromatography (Preparative C18 125Å bulk packing material, water:methanol, gradient elution 0:100 to 100:0) to afford the sub-title compound (0.36g).

NMR δH (d_6-DMSO) 1.82-2.01 (2H, m), 2.14-2.19 (2H, m), 2.65 (3H, d), 3.74-3.76 (1H, m), 6.90 (1H , s), 7.48 (1H, s), 8.34 (1H, s), 8.60 (1H, q).

c) [3a*R*-(3aα,4α(*S),6α,6aα)]-*N*-[4-Amino-1-(1-methylamino)carbonyl-4-oxo-butyl]-6-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolopyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxol-4-yl-carboxamide**

Prepared according to the method of example 20, step a) using the product of step b) and the product of example 1, step g).

MS (APCI) 592 ($M+H^+$, 100%).

d) [1*S*-(1α,2β,3β,4α)]-*N*-[4-Amino-1-[(methylamino)carbonyl]-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of example 1, step i) using the product of step c).

MS (APCI) 552 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.91 (3H,t), 0.98 (3H,t), 1.36 (2H,sex), 1.62 (2H,quin), 1.69 (2H, sex), 1.66-1.74 (1H, m), 1.80-1.95 (1H, m), 2.03 (2H, t), 2.15-2.25 (1H, m), 2.30-2.40 (1H, m), 2.60 (3H, d), 2.89-2.90 (1H, m), 3.06-3.18 2H, m), 3. (2H, q), 4.12-4.16 (1H, m), 4.19-4.21 (1H, m), 4.39-4.42 (1H, m), 4.90-5.00 (1H, m), 5.03 (1H, d), 5.15 (1H, d), 6.71 (1H, s), 7.23 (1H, s), 7.85 (1H, q), 8.07 (1H, d), 8.99 (1H, t)

Example 65
[1*S*-(1α(*R),2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-3-hydroxy-propyl)-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of example 59, step a) using the product of example 2 and (2*S*)-2-amino-4-hydroxy-butanamide (prepared as described by R. M. Khomutov *et al*, *Chem. Abs.*, **58**, 13944)

MS (APCI) 511 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.99 (1H, t), 8.02 (1H, d), 7.29 (1H, s), 7.05 (1H, s), 5.16 (1H, d), 5.03 (1H, d), 5.00-4.92 (1H, m), 4.46 (1H, t), 4.43-4.37 (1H, m), 4.33-4.26 (1H, m), 4.18-4.12 (1H, m), 3.50 (2H, q), 3.43-3.37 (2H, m), 3.20-3.02 (2H, m), 2.94-2.87 (1H, m), 2.42-2.32 (1H, m), 2.28-2.15 (1H, m), 1.90-1.79 (1H, m), 1.77-1.55 (5H, m), 1.44-1.29 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 66

[1*S*-(1α(*R),2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-hydroxy-ethyl)-2,3-dihydroxy-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl] - cyclopentanecarboxamide**

a) [3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step g) using the product of example 1, step f) and 4-phenylbutylamine.

MS (APCI) 527 ($M+H^+$, 100%)

b) [3a*R*-(3aα,4α,6α(*S),6aα)]-*N*-[1-(Aminocarbonyl)-2-hydroxy-ethyl)-tetrahydro-2,2-dimethyl-6-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 59, step a) using the product of step a) and (2*S*)-2-amino-3-hydroxy-propanamide, hydrochloride.

MS (APCI) 613 ($M+H^+$, 100%)

c) [1*S*-(1α(*R),2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-hydroxy-ethyl)-2,3-dihydroxy-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl] - cyclopentanecarboxamide**

Prepared according to the method of example 1, step (i) using the product from step (b).

MS (APCI) 573 ($M+H^+$, 100%)

NMR δH (d_6-DMSO) 9.01 (1H, t), 7.88 (1H, d), 7.27-7.13 (7H, m), 5.17 (1H, d), 5.07 (1H, d), 4.97-4.95 (1H, m), 4.87-4.84 (1H, m), 4.39-4.37 (1H, m), 4.26-4.24 (1H, m), 4.15-4.13 (1H, m), 3.60-3.51 (4H, m), 3.10-3.05 (2H, m), 2.93-2.29 (1H, m), 2.61 (2H, m), 2.34 (1H, m), 2.25 (1H, m), 1.71-1.63 (6H, m), 0.98 (3H, t).

Example 67

1*S*-[1α,2β,3β,4α(1*S,2*R**)]-*N*-[(Aminocarbonyl)methyl]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

a) **[3a*R*-(3aα,4α,6α(1*R**,2*S**),6aα]-*N*-[(Aminocarbonyl)methyl]-tetrahydro-2,2-dimethyl-6-[7-[2-(phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 59, step a) using the product of example 34, step a) and glycinamide hydrochloride.

MS (APCI) 567 ($M+H^+$)

b) **1*S*-[1α,2β,3β,4α(1*S**,2*R**)]-*N*-[(Aminocarbonyl)methyl]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

Prepared according to the method of example 26, step b) using the product of step a).

MS (APCI) 527 ($M+H^+$)

NMR δH (d_6-DMSO) 9.31 (1H, d), 8.04 (1H, br t), 7.26-7.11 (6H, m), 7.00 (1H, br s), 5.12 (1H, d), 5.00 (1H, d), 4.94 (1H, m), 4.37 (1H, m), 4.10 (1H, m), 3.63 (2H, m), 3.16 (1H, m), 2.91 (1H, m), 2.81 (2H, m), 2.33-2.18(2H, m), 2.08 (1H, m), 1.47 (1H, m), 1.28 (1H, m), 0.76 (3H, t).

Example 68

[1*S*-(1α(*R),2β,3β,4α)]-*N*-[(1-Aminocarbonyl)-4-(methylamino)-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

a) **(2*S*)-2-Amino-5-(methylamino)-5-oxo-pentanamide**

N,N-Diisopropylethylamine (2.0ml) was added to a solution of (4*S*)-5-amino-4-[[(1,1-dimethylethoxy)carbonyl]amino]-5-oxo-pentanoic acid (0.49g), bromo-tris-pyrrolidino-

phosphonium hexafluorophosphate (1.20g) and methylamine (0.16g) in acetonitrile (20ml). The reaction mixture was stirred at room temperature for 2 hours then concentrated. The residue was taken into 4M HCl in 1,4-dioxane (20ml), stirred for 4 hours then concentrated. Purification (Preparative C18 125Å bulk packing material, water:methanol, gradient elution 0:100 to 100:0) gave the sub-title compound (0.48g).

NMR δH (d_6-DMSO) 8.24 (2H, br s), 8.00-7.98 (1H, m), 7.95 (1H, be s), 7.58 (1H, br s), 3.74 (1H, br s), 2.56 (3H, d), 2.26-2.12 (2H, m), 2.10-1.92 (2H, m).

b) [3αR-[3aα,4α(S*),6α,6aα]]-N-[1-(Aminocarbonyl)-4-(methylamino)-4-oxobutyl]-6-[7-(butylamino)-5-(propylthio)-3H-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide

Prepared according to the method of example 20, step a) using the product of step a) and the product of example 1, step g).

MS (APCI) 593 ($M+H^+$,100%)

c) [1*S*-(1α(*R),2β,3β,4α)]-*N*-[(1-Aminocarbonyl)-4-(methylamino)-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product from step b).

MS (APCI) 552 ($M+H^+$,100%)

NMR δH (d_6-DMSO) 8.99 (1H, t), 8.02 (1H, d), 7.69 (1H, q), 7.33 (1H, s), 7.08 (1H, s), 5.15 (1H, br s), 5.03 (1H, br s), 4.97-4.94 (1H, m), 4.40 (1H, br s), 4.21-4.16 (1H, br s), 4.16-4.14 (1H, br s), 3.49 (2H, q), 3.13-3.06 (2H, m), 2.91-2.89 (1H, m), 2.53 (3H, d), 2.38-2.35 (1H, m), 2.23 (1H, m), 2.06 (2H, t), 1.90-1.89 (1H, m), 1.77-1.66 (1H, m), 1.74 (2H, sextuplet), 1.63 (2H, quint), 1.34 (2H, sextuplet), 0.99 (3H, t), 0.91 (3H, t).

Example 69

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of example 66, step a).

MS (APCI) 487 ($M+H^+$)

NMR δH (d_6-DMSO) 9.00 (1H, t), 7.28-7.12 (5H, m), 5.18-5.14 (1H, m), 5.04-4.95 (1H, m), 4.43-4.37 (1H, m), 4.22-4.21 (1H, m), 3.53-3.51 (1H, m), 3.12-2.99 (2H, m), 2.85-2.78 (1H, m), 2.61 (2H, m), 2.49-2.27 (2H, m), 1.74-1.63 (6H, m), 0.98 (3H, t).

Example 70

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) [3a*R*-(3aα,4α,6α,6aα)]-Tetrahydro-2,2-dimethyl-6-[7-[(1-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1 step g) using the product of example 1, step f) and 1-phenylcyclopropylamine.

MS (APCI) 511 ($M+H^+$,100%)

b) [1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 471 ($M+H^+$)

NMR δH (d_6-DMSO) 9.79 (1H, s), 7.27-7.13 (5H, m), 5.18 (2H, br s), 5.00 (1H, q), 4.40 (1H, br s), 4.22-4.20 (1H, m), 2.88-2.80 (3H, m), 2.49-2.30 (2H, m), 1.47-1.35 (6H, m), 0.77 (3H, t).

Example 71

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2,3-dihydroxypropyl)-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 2 and 3-amino-1,2-propanediol.

MS (APCI) 484 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.98 and 8.60 (1H, t), 7.89 (1H, m), 5.12 (1H, d), 5.00-4.90 (2H, m), 4.76 and 4.75 (1H, d), 4.52 (1H, t), 4.42 (1H, m), 4.12 (1H, m), 3.49 and 3.90 (3H, m), 3.32-3.19 (3H, m), 3.18-2.98 (3H, m), 2.83 (1H, m), 2.40-2.18 (2H, m), 1.71 (2H, sextet), 1.63 (2H, quintet), 1.35 (2H, sextet), 0.99 (3H, t), 0.91 (3H, t)

Example 72

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-hydroxy-2-(4-hydroxyphenyl)-ethyl]-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 2 and α-(aminomethyl)-4-hydroxybenzylalcohol hydrochloride.

NMR δH (d_6-DMSO) 9.24 (1H, s), 8.98 (1H, t), 7.91 (1H, m), 7.12 (2H, t), 6.70 (2H, m), 5.27 (1H, m), 5.12 (1H, d), 4.51 (1H, m), 4.42 (1H, m), 4.10 (1H, m), 3.51 (2H, q), 3.10 (3H, m), 2.82 (1H, m), 2.30 (1H, m), 2.20 (1H, m), 1.72 (4H, m), 1.36 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 73

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-hydroxy-2-(3-hydroxyphenyl)-ethyl]-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 2 and α-(aminomethyl)-3-hydroxybenzylalcohol hydrochloride.

NMR δH (d_6-DMSO) 9.27 (1H, s), 8.98 (1H, t), 7.97 (1H, t), 7.08 (1H, m), 6.72 (2H, m), 6.62 (1H, d), 5.38 (1H, m), 5.12 (1H, d), 4.95 (2H, m), 4.52 (1H, m),.4.45 (1H,m), 4.12 (1H, m), 3.50 (2H, q), 3.30 (1H, m), 3.09 (3H, m), 2.82 (1H, m), 1.71 (2H, m), 1.60 (2H, m), 1.35 (2H, m), .0.98 (3H, t), 0.90 (3H, t).

Example 74

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(4-hydroxy-3-methoxyphenyl)-methyl]-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 2 and 4-hydroxy-3-methoxybenzylamine hydrochloride.

NMR δH (d_6-DMSO) 8.81 (1H, s), 8.98 (1H, t), 8.33 (1H, t), 6.83 (1H, d), 6.68 (2H, m), 5.16 (1H, d), 5.00 (1H, d), 4.98 (1H, t), 4.45 (1H, m), 4.20 (3H, m), 3.72 (3H, s), 3.50 (2H, q), 3.09 (2H, m), 2.84 (1H, m), 2.32 (2H, m), 1.70 (2H, m), 1.59 (2H, m), 1.35 (2H, m), 0.97 (3H, t), 0.90 (3H, t).

Example 75

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(4-hydroxyphenyl)-methyl]-cyclopentanecarboxamide.

a) **4-Hydroxybenzylamine hydrobromide**

4-Methoxybenzylamine (1.00ml) in 48% HBr aq (10ml) and heated at reflux for 10 hours. The cooled reaction mixture was filtered to give the sub-title compound (2.25g).

NMR δH (d_6-DMSO) 9.59 (1H, s), 8.01 (3H, br s), 7.27 (2H, d), 6.80 (2H, d), 3.91 (3H, d).

b) **[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(4-hydroxyphenyl)-methyl]-cyclopentanecarboxamide.**

Prepared according to the method of example 59, step a) using the product of example 2 and product of step a).

NMR δH (d_6-DMSO) 9.26 (1H, s), 8.99 (1H, t), 8.32 (1H, t), 7.08 (2H, d), 6.70 (2H, d), 5.14 (1H, d), 5.00 (1H, d), 4.95 (1H, m), 4.46 (1H, m), 4.19 (3H, m), 3.51 (2H, q), 3.10 (1H, m), 2.83 (1H, m), 2.31 (2H, m), 1.69 (2H, m), 1.60 (2H, m), 1.36 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 76

[1*S*-[1α,2β,3β,4α (1*R,2*S**)]]-2,3-Dihydroxy-*N*-(2-hydroxyethyl)-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

a) [3a*R*-[3aα,4α,6α(1*S,2*R**),6aα]]-Tetrahydro-*N*-(2-hydroxyethyl)-2,2-dimethyl-6-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 20, step a) using the product of example 56, step a).

MS (APCI) 554 ($M+H^+$, 100%).

b) [1*S*-[1α,2β,3β,4α (1*R,2*S**)]]-2,3-Dihydroxy-*N*-(2-hydroxyethyl)-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 514 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.35 and 8.96 (1H, m), 8.02 (1H, t), 7.31-7.15 (5H, m), 5.29 (2H, br s), 4.96 (1H, m), 4.78 (1H, br s), 4.41 (1H, m), 4.10 (1H, m), 3.42 (2H, m), 3.25-2.74 and 3.82 (6H, m), 2.40-2.10 (3H, m), 1.80-1.28 (4H, m), 0.81 and 0.99 (3H, t)

Example 77

[1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-*N*-(2-hydroxyethyl)-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

a) **[3a*R*-[3aα,4α,6α(1*R**,2*S**),6aα]]-Tetrahydro-*N*-(2-hydroxyethyl)-2,2-dimethyl-6-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 20, step a) using the product of example 34, step a).

MS (APCI) 554 ($M+H^+$, 100%).

b) **[1*S*-[1α,2β,3β,4α (1*S**,2*R**)]]-2,3-Dihydroxy-*N*-(2-hydroxyethyl)-4-[7-(2-phenylcyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 514 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.35 and 8.95 (1H, d), 7.92 (1H, t), 7.31-7.15 (5H, m), 5.12 (1H, d) 5.00-4.92 (2H, m), 4.67 (1H, t), 4.43 (1H, m), 4.10 (1H, q), 3.41 (2H, q), 3.21-3.12 and 3.85 (3H, m), 3.01-2.72 (3H, m), 2.40-2.10 (3H, m), 1.77-1.42 (3H, m), 1.32 (1H, m), 0.81 and 0.99 (3H, t)

Example 78

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(2-hydroxy-5-nitrophenyl)methyl]-cyclopentanecarboxamide

a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-*N*-[(2-hydroxy-5-nitrophenyl)methyl]-2,2-dimethyl-4*H*-cyclopenta-1,3-diox le-4-carboxamide**

Prepared according to the method of example 59, step a) using the product of example 1, step g) and 2-(aminomethyl)-4-nitrophenol.

MS (APCI) 601 ($M+H^+$, 100%).

b) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(2-hydroxy-5-nitrophenyl)methyl]-cyclopentanecarboxamide

Prepared according to the method of example 1 step i) using the product of step a).

MS (APCI) 561 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 0.88-0.98 (6H, m), 1.31-1.38 (2H, m), 1.57-1.71 (4H, m), 2.27-2.41 (2H, m), 2.90-2.93 (1H, m), 3.04-3.10 (2H, m), 3.46-3.52 (1H, m), 4.17-4.18 (1H, m), 4.27-4.29 (2H, m), 4.42-4.46 (1H, m), 4.97-5.06 (2H, m), 5.19 (1H, d), 6.95-6.99 (1H, m), 8.03-8.06 (2H, m), 8.54 (1H, t), 8.99 (1H, t).

Example 79

[1*S*-[1α,2β,3β,4α (*trans*)]]-2,3-Dihydroxy-*N*-(2-Hydroxyethyl)-4-[5-[[(4-trifluoromethyl)phenyl]thio]-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboamide

Prepared according to the method of example 20, step a) using the product of example 5.

MS (APCI) 616 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.44 (1H, d), 7.93-7.60 (4H, m), 7.29-7.06 (5H, m), 5.11 (1H, d), 4.95-4.91 (2H, m), 4.67 (1H, t), 4.38-4.34 (1H, m), 4.04 (1H, q), 3.41 (2H, q), 3.16 (2H, q), 3.08-3.04 (1H, m), 2.80-2.75 (1H, m), 2.35-2.17 (3H, m), 1.41-1.37 (1H, m), 1.13 (1H, q).

Example 80

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(3,4-dihydroxyphenyl)methyl]-cyclopentanecarboxamide.

Prepared according to the method of example 20, step a) using the product of example 2 and 3,4-dihydroxybenzylamine hydrochloride.

NMR δH (d_6-DMSO) 9.05 (1H, t), 8.75 (1H, br s), 8.29 (1H, br s), 6.65 (2H, m), 6.52 (1H, d), 4.99 (2H, m), 4.47 (1H, m), 4.13 (2H, m), 3.51 (2H, q), 3.32 (2H, s), 3.10 (2H, m), 2.80 (1H, m), 2.30 (2H, m), 1.69 (2H, m), 1.58 (2H, m), 1.36 (2H, m), 0.99 (3H, t), 0.91 (3H, t).

Example 81

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(2-hydroxyphenyl)methyl]-cyclopentanecarboxamide.

a) **2-Hydroxyphenylmethylamine, hydrobromide**

Prepared according to the method of example 75, step a) using 2-methoxybenzylamine.

NMR δH (d_6-DMSO) 9.55 (1H, s), 8.99 (1H, t), 8.36 (1H, t), 7.10 (1H, m), 6.77 (1H, m), 5.16 (1H,d), 5.03 (1H, d), 4.95 (1H, d), 4.42 (1H, m), 4.24 (2H, m), 4.17 (1H, m), 3.90 (2H, q), 3.09 (2H, m), 2.85 (1H, m), 2.35 (2H, m), 1.69 (2H, m), 1.60 (2H, m), 1.36 (3H, m), 0.98 (3H, m), 0.91 (3H, m).

b) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(2-hydroxyphenyl)methyl]-cyclopentanecarboxamide.

Prepared according to the method of example 59, step a) using the product of example 2 and product of step a).

NMR δH (d_6-DMSO) 9.55 (1H, s), 8.99 (1H, t), 8.36 (1H, t), 7.10 (2H, d), 6.77 (2H, d), 5.16 (1H, d), 5.03 (1H, d), 4.95 (1H, m), 4.42 (1H, m), 4.17 (3H, m), 3.51 (2H, q), 3.09

(2H, m), 2.85 (1H, m), 2.35 (2H, m), 1.69 (2H, m), 1.60 (2H, m), 1.36 (2H, m), 0.98 (3H, t), 0.91 (3H, t).

Example 82

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-*N*-[2-hydroxyethyl]-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 66, step a) and ethanolamine, followed by the method of example 1, step i).

MS (APCI) 530 ($M+H^+$)

NMR δH (d_6-DMSO) 9.01 (1H, t), 7.92-7.90 (1H, m), 7.27-7.15 (5H, m), 5.12 (1H, d), 4.98-4.93 (2H, m), 4.67 (1H, t), 4.43-4.41 (1H, m), 4.10-4.09 (1H, m), 3.53-3.51 (2H, m), 3.43-3.38 (2H, m), 3.17-3.05 (4H, m), 2.78-2.77 (1H, m), 2.63-2.59 (2H, m), 2.24 (2H, m), 1.71-1.63 (6H, m), 0.98 (3H, t).

Example 83

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]- 2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide

a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-*N*-(2-hydroxyethyl)-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 59, step a) using the product of example 3, step a).

MS (APCI) 478 ($M+H^+$)

a) **[1*S*-(1α,2β,3β,4α)]-4-[7-Cyclopropylamino-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 438 ($M+H^+$)

NMR δH (d_6-DMSO) 9.10 (1H, d), 7.93 (1H, t), 5.01-4.90 (1H, m), 4.51-4.40 (1H, m), 4.16-4.11 (1H, m), 3.42 (2H, t), 3.25-3.00 (5H, m), 2.76 (1H, td), 2.39-2.21 (2H, m), 1.80-1.65 (2H, m), 0.98 (3H, t), 0.90-0.65 (4H, m).

Example 84

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(3-hydroxyphenyl)methyl]-cyclopentanecarboxamide

Prepared according to the method of example 59, step a) using the product of example 2 and 3-hydroxyphenylmethylamine.

MS (APCI) 516 ($M+H^+$)

NMR δH (d_6-DMSO) 9.28 (1H, s), 8.59 (1H, t), 8.36 (1H, t), 7.05 (1H,t), 6.64-6.51 (3H, m), 5.11 (1H, d), 4.97 (1H,d), 4.94 (1H, m), 4.40 (1H, m), 4.18 (2H,d), 4.12 (1H, m), 3.46 (2H, q), 3.10-3.00 (2H, m), 2.85-2.75 (1H, m), 2.40-2.30 (1H,m), 2.28-2.20 (1H, m), 1.68-1.63 (2H, m), 1.58-1.54 (2H, m), 0.94 (3H, t), 0.87 (3H, t).

Example 85

[1*S*-[1α,2β,3β,4α(1*S,2*R**)]]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

a) [1*R*-[1α(*S),2β]]-*N*-[2-(4-Chlorophenyl)cyclopropyl]-2-methoxy-2-phenyl-acetamide and [1*S*-[1α(*R**),2β]]-*N*-[2-(4-Chlorophenyl)cyclopropyl]-2-methoxy-2-phenyl-acetamide**

Oxalyl chloride (4.00ml) was added to a solution of (*S*)-α-methoxyphenylacetic acid (2.00g) in dichloromethane (100ml)/DMF (10ml). The reaction mixture was stirred at room temperature for 4 hours then concentrated and the residue azeotroped with dichloromethane (3x10ml). The resulting oil was taken into dichloromethane (4ml) and treated with a solution of 2-(4-chlorophenyl)cyclopropylamine (Prepared as described by C Kaiser *etal* J. Med. Pharm. Bul., 1962, 5, 1243) (1.86g) in pyridine (8ml). The reaction mixture was stirred at room temperature for 30 minutes then partitioned between

dichloromethane (500ml) and water (500ml). The organic phase was dried and concentrated and the residue purified (SiO_2, isohexane:ethyl acetate:acetic acid 66:33:1) to afford [1*S*-[1α(*R**),2β]]-*N*-[2-(4-Chlorophenyl)cyclopropyl]-2-methoxy-2-phenyl-acetamide (1.23g)

MS (APCI, negative ionization) 314 ($M-H^+$, 100%)

Further elution of the column gave [1*R*-[1α(*S**),2β]]-*N*-[2-(4-Chlorophenyl)cyclopropyl]-2-methoxy-2-phenyl-acetamide (1.40g).

MS (APCI, negative ionization) 314 ($M-H^+$, 100%).

b) (1*R*-*trans*)-2-(4-Chlorophenyl)-cyclopropylamine

A solution of [1*R*-[1α(*S**),2β]]-*N*-[2-(4-Chlorophenyl)cyclopropyl]-2-methoxy-2-phenyl-acetamide (1.10g) (prepared as described in step a)) in 1,4-dioxane (20ml) containing 5M HCl (aq) (40ml) was heated at reflux for 18 hours. The reaction was concentrated and the residue partitioned between water and diethyl ether. The aqueous phase was treated with 2M aqueous sodium hydroxide solution (100ml) then extracted with diethyl ether (2x100ml). The organic phase was concentrated to afford the sub-title compound (0.55g).

Optical rotation -138.3° (c=0.2, methanol).

c) [3a*R*-[3aα,4α,6α(1*R,2*S**),6aα]]-6-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 1, step g) using the product of example 1, step f) and the product of step b).

MS (APCI) 547, 545 ($M+H^+$), 545 (100%).

d) [1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i) using the product of step c).

MS (APCI) 507, 505 ($M+H^+$), 505 (100%).

NMR δH (d_6-DMSO) 9.37 (1H, d), 7.33 (2H, d), 7.22 (2H, d), 5.01 (1H, q), 4.41 (1H, q), 4.22 (1H, t), 3.18-3.15 (1H, m), 2.96-2.90 (1H, m), 2.87-2.80 (2H, m), 2.50-2.45 (1H, m), 2.38-2.30 (1H, m), 2.15-2.11 (1H, m), 1.56-1.47 (3H, m), 1.38-1.33 (1H, m), 0.81 (3H, t).

Example 86

[1*S*-[1α,2β,3β,4α(1*S,2*R**)]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide**

Prepared according to the method of example 63, step a) using the product of example 85, step d).

MS (APCI) 506, 504 ($M+H^+$), 504 (100%).

NMR δH (d_6-DMSO) 9.36 (1H, d), 7.38 (1H, s), 7.34 (2H, d), 7.22 (2H, m), 6.92 (1H, s), 5.14 (1H, d), 5.02-.4.94 (2H, m), 4.42-4.39 (1H, m), 4.13-4.11 (1H, m), 3.19-2.95 (1H, m), 2.92-2.74 (3H, m), 2.35-2.24 (2H, m), 2.15-2.11 (1H, m), 1.57-1.45 (3H, m), 1.38-1.33 (1H, m), 0.81 (3H, t).

Example 87

[1*S*-[1α,2β,3β,4α(1*R,2*S**)]]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

a) (1*S*-*trans*)-2-(4-Chlorophenyl)cyclopropylamine

Prepared according to the method of example 85, step b) using [1*S*-[1α(*R**),2β]]-*N*-[2-(4-Chlorophenyl)cyclopropyl]-2-methoxy-2-phenyl-acetamide (the product of example 85, step a).

Optical rotation +159.0° (c=0.2, methanol).

b) [3a*R*-[3aα,4α,6α(1*S,2*R**),6aα]]-6-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 1, step g) using the product of example 1, step f) and the product of step a).

MS (APCI) 547, 545 ($M+H^+$), 545 (100%).

b) [1*S*-[1α,2β,3β,4α (1*R,2*S**)]]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i) using the product of step b).

MS (APCI) 507, 505 ($M+H^+$), 505 (100%).

NMR δH (d_6-DMSO) 12.43 (1h, br s), 9.36 (1H, d), 7.34 (2H, d), 7.23 (2H, d), 5.19-5.16(2H, m), 5.01 (1H, q), 4.43-4.38 (1H, m), 4.23-4.20 (1H, m), 3.18-3.15 (1H, m), 2.92-2.80 (3H, m), 2.50-2.27 (2H, m), 2.15-2.11 (1H, m), 1.56-1.46 (3H, m), 1.38-1.33 (1H, m), 0.81 (3H, t).

Example 88

[1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]- -cyclopentanecarboxylic acid**

a) 4,6-Dihydroxy-2-(methylthio)-pyrimidine

Prepared according to the method of example 1, step a), using iodomethane.

MS (APCI) 159 ($M+H^+$, 100%).

b) 4,6-Dihydroxy-2-(methylthio)-5-nitro-pyrimidine

Prepared according to the method of example 1, step b), using the product of step a).

MS (APCI, negative ionization) 202 ($M-H^+$, 100%).

c) 4,6-Dichloro-2-(methylthio)-5-nitro-pyrimidine

Prepared according to the method of example 1, step c), using the product of step b).

m. pt. 59°C

d) [3a*S*-(3aα,4β,7β,7aα)]-5-[6-Chloro-2-(methylthio)-5-nitro-pyrimidin-4-yl]-tetrahydro-2,2-dimethyl-4,7-methano-1,3-dioxolo[4,5-*c*]pyridin-6(3a*H*)-one

Prepared according to the method of example 1, step d), using the product of step c).

MS (APCI) 389, 387 ($M+H^+$), 387 (100%).

e) [3a*R*-(3aα,4α,6α,6aα)]-6-[[5-Amino-6-chloro-2-(methylthio)-4-pyrimidinyl]amino]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step e), using the product of step d).

MS (APCI) 375 ($M+H^+$, 100%).

f) [3a*R*-(3aα,4α,6α,6aα))]-6-[7-Chloro-5-(methylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 1, step f), using the product of step e).

MS (APCI) 388, 386 ($M+H^+$), 386 (100%).

g) [3a*R*-[3aα,4α,6α(*R,*S**),6aα]]-Tetrahydro-2,2-dimethyl-6-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 34, step a) using the product of step f).

MS (APCI) 483 ($M+H^+$, 100%).

h) [1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i) using the product of step g).

MS (APCI) 443 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 7.31-7.15 (5H, m), 5.00 (1H, q), 4.43 (1H, q), 4.19 (1H, t), 3.19 (1H, m), 2.68 (1H, m), 2.37 (1H, m), 2.32 (3H, s), 2.12 (1H, m), 1.87 (2H, s), 1.50 (1H, m), 1.33 (1H, m).

Example 89
[1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

a) [3a*R*-[3aα,4α,6α(*R,*S**),6aα]]-Tetrahydro-2,2-dimethyl-6-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-4*H*-cyclopenta-1,3-dioxole-4-carboxamide**

Prepared according to the method of example 1, step h) using the product of example 88, step g).

MS (APCI) 481 ($M+H^+$, 100%).

b) [1*S*-[1α,2β,3β,4α (1*S,2*R**)]]-2,3-Dihydroxy-4-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide**

Prepared according to the method of example 1, step i) using the product of step a).

MS (APCI) 442 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 9.36 (1H, d), 7.38 (1H, s), 7.31-7.15 (5H, m), 6.92 (1H, d), 5.12 (1H, d), 4.98 (2H, m), 4.41 (1H, q), 4.13 (1H, q), 3.19 (2H, m), 2.76 (2H, m), 2.25 (2H, m), 2.13 (1H, m), 1.50 (1H, m), 1.32 (1H, m).

Example 90

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy 4-[7-[2-(phenylamino)ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step g,) using the product of example 1, step f) and 2-(phenylamino)ethylamine, followed by the method of example 1, step i).

MS (APCI) 474 ($M+H^+$, 100%).

Example 91

a) [3a*R*-(3aα,4α,6α,6aα)]-6-[7-(Butylamino)-5-[(1-methyl)ethylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

Prepared according to the method of example 11, step b), using the product of example 13, step a) and 2-propanethiol.

MS (APCI) 451 ($M+H^+$, 100%).

b) [1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[(1-methyl)ethylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide

Prepared according to the method of example 1, step h), followed by the method of example 1, step i) using the product of step a).

MS (APCI) 410 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 8.97 (1H, t), 7.36 (1H, s), 6.91 (1H, s), 5.11 (1H, d), 4.93 (2H, m), 4.39 (1H, m), 4.10 (1H, m), 3,91 (1H, m), 3.50 (2H, m), 2.33 (1H, m), 2.35-2.21 (2H, m), 1.62 (2H, m), 1.39 (8H, m), 0.91 (3H, m).

Example 92

[1*S*-(1α,2β,3β,4α)]-4-[7-[2-(4-Chlorophenyl)-ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid

a) **[3a*R*-(3aα,4α,6α,6aα)]-6-[7-[2-(4-Chlorophenyl)-ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 1, step g), using the product of example 1, step f) and 2-(4-chlorophenyl)ethylamine.

MS (APCI) 535, 533 ($M+H^+$), 533 (100%).

b) **[1*S*-(1α,2β,3β,4α)]-4-[7-[2-(4-Chlorophenyl)-ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid**

Prepared according to the method of example 1, step i), using the product of step a)

(APCI) 495, 493 ($M+H^+$), 493 (100%).

Example 93

[1*S*-[1α,2β,3β,4α(*E*)]]-2,3-Dihydroxy-4-[7-(3-iodo-prop-2-enylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

a) **[3a*R*-[3aα,4α,6α(*E*),6aα]]-6-[7-(3-Tributylstannyl-prop-2-enylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-tetrahydro-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid**

Prepared according to the method of example 1, step g), using the product of example 1, step f) and (3-tributylstannyl)-prop-2-enylamine.

NMR δH ($CDCl_3$) 6.15 (1H, d), 5.92 (1H, d t), 5.65 (1H, m), 5.52 (1H, m), 5.13 (1H, m), 4.39 (1H, m), 3.15 (2H, m), 2.95 (2H, m), 2.60 (1H, m), 1.82 (2H, m), 1.58 (3H, s), 1.62-1.45 (9H, m), 1.39-1.28 (8H, m), 1.91 (3H, t), 1.00-0.81 (15H, m).

b) [3a*R*-[3aα,4α,6α(*E*),6aα]]-Tetrahydro-6-[7-(3-iodo-prop-2-enylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-4-carboxylic acid

A solution of iodine (0.18g) in THF (1ml) was added to a solution of the product of step a) (0.45g) in THF (5ml) at 0°C. After 10 minutes the reaction mixture was partitioned between ethyl acetate (50ml) and 10% sodium metabisulfite (aq) (50ml). The organic layer was dried and concentrated. Purification (SiO_2, diethyl ether as eluant) gave the subtitle compound (0.21g).

NMR δH ($CDCl_3$) 7.94 (1H, t), 6.43 (1H, d t), 6.30 (1H, d), 5.78 (1H, d), 5.70 (1H, d), 5.12 (1H, d), 4.20 (1H, m), 3.56 (1H, m), 3.26-3.01 (4H, m), 2.62 (1H, m), 1.83 (2H, m), 1.65 (3H, s), 1.45 (3H, s), 1.10-0.81 (3H, t).

c) [1*S*-[1α,2β,3β,4α(*E*)]]-2,3-Dihydroxy 4-[7-(3-iodo-prop-2-enylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid

Prepared according to the method of example 1, step i), using the product of step b).

MS (APCI) 521 ($M+H^+$, 100%).

NMR δH (d_6-DMSO) 6.65 (1H, d t), 6.45 (1H, d), 4.98 (1H, q), 4.40 (1H, m), 4.26 (1H, m), 4.08 (2H, d), 3.20-3.00 (2H, m), 2.75-2.65 (1H, m), 2.53-2.22 (2H, m), 1.68 (2H, m), 0.99 (3H, t).

Pharmacological data

The preparation for the assay of the P_{2T}-receptor agonist/antagonist activity in washed human platelets for the compounds of the invention was carried out as follows.

Human venous blood (100 ml) was divided equally between 3 tubes, each containing 3.2% trisodium citrate (4 ml) as anti-coagulant. The tubes were centrifuged for 15 minutes at 240G to obtain a platelet-rich plasma (PRP) to which 300 ng/ml prostacyclin was added to stabilize the platelets during the washing procedure. Red cell free PRP was obtained by centrifugation for 10 minutes at 125G followed by further centrifugation for 15 minutes at 640G. The supernatant was discarded and the platelet pellet resuspended in modified,

Calcium Free Tyrode solution (10 ml) (CFT), composition: NaCl 137mM, $NaHCO_3$ 11.9mM, NaH_2PO_4 0.4mM, KCl 2.7 mM, $MgCl_2$ 1.1 mM, dextrose 5.6 mM, gassed with 95% O_2/5% CO_2 and maintained at 37°C. Following addition of a further 300 ng/ml PGI_2, the pooled suspension was centrifuged once more for 15 minutes at 640G. The supernatant was discarded and the platelets resuspended initially in 10 ml CFT with further CFT added to adjust the final platelet count to $2x10^5$/ml. This final suspension was stored in a 60 ml syringe at 3°C with air excluded. To allow recovery from PGI_2-inhibition of normal function, platelets were used in aggregation studies no sooner than 2 hours after final resuspension.

In all studies, 3 ml aliquots of platelet suspension were added to tubes containing $CaCl_2$ solution (60 µl of 50 mM solution with a final concentration of 1mM). Human fibrinogen (Sigma, F 4883) and 8-sulphophenyltheophylline (8-SPT which was used to block any P_1-agonist activity of compounds) were added to give final concentrations of 0.2 mg/ml (60 µl of 10 mg/ml solution of clottable protein in saline) and 300 nM (10 µl of 15 mM solution in 6% glucose), respectively. Platelets or buffer as appropriate were added in a volume of 150 µl to the individual wells of a 96 well plate. All measurements were made in triplicate in platelets from each donor.

The agonist/antagonist potency was assessed as follows.

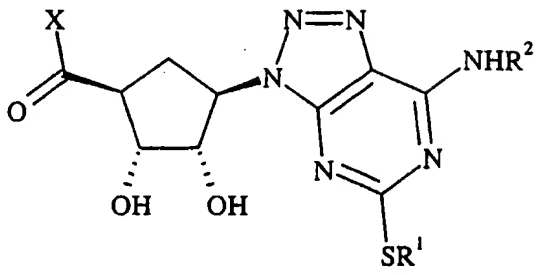
Aggregation responses in 96 well plates were measured using the change in absorbance given by the plate reader at 660 nm. Either a Bio-Tec Ceres 900C or a Dynatech MRX were used as the plate reader.

The absorbance of each well in the plate was read at 660 nm to establish a baseline figure. Saline or the appropriate solution of test compound was added to each well in a volume of 10 µl to give a final concentration of 0, 0.01, 0.1, 1, 10 or 100 mM. The plate was then shaken for 5 min on an orbital shaker on setting 10 and the absorbance read at 660 nm. Aggregation at this point was indicative of agonist activity of the test compound. Saline or ADP (30 mM; 10 µl of 450 mM) was then added to each well and the plate shaken for a further 5 min before reading the absorbance again at 660 nm.

Antagonist potency was estimated as a % inhibition of the control ADP response to obtain an IC_{50}. Compounds of the invention have pIC_{50} values of more than 5.0

Claims

1. A compound of formula (I):



(I)

wherein;

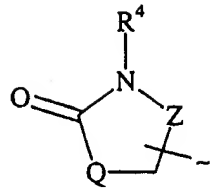
X is OH or NHR^3;

R^1 is C_{1-6}-alkyl, C_{3-8}-cycloalkyl or a phenyl group, each group being optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl (itself optionally substituted by one or more halogen atoms);

R^2 is C_{1-8}-alkyl or C_{2-8}-alkenyl each of which is optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl, C_{3-8}-cycloalkyl, aryl and/or C_{1-6}-alkyl groups; or R^2 is a C_{3-8}-cycloalkyl group optionally substituted by one or more halogen atoms and/or OR^4, NR^4R^5, C_{1-6}-thioalkyl, phenyl and/or C_{1-6}-alkyl groups; the optional phenyl substituent being further optionally substituted by one or more halogen atoms and/or NO_2, $C(O)R^4$, OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl groups;

R^3 is hydrogen or C_{1-6}-alkyl substituted by one or more hydroxy and/or phenyl groups and optionally by one or more halogen atoms, wherein the phenyl group is substituted by one or more hydroxy groups and optionally substituted by one or more halogen atoms and/or NO_2, $C(O)R^4$, OR^4, NR^4R^5, C_{1-6}-thioalkyl and/or C_{1-6}-alkyl groups, or R^3 is a C_{1-6}-alkyl group substituted by a $C(O)NR^4R^5$ or a COOH group and optionally by one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, wherein the alkyl group is optionally substituted by one or more hydroxy and/or phenyl groups and wherein the phenyl group is optionally substituted as defined above for R^3; or

R^3 is a lactam ring of formula (i):

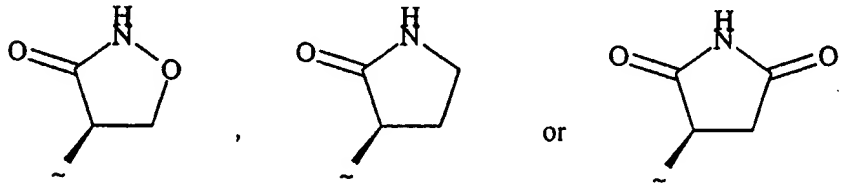


wherein Q is a $(CH_2)_m$ moiety wherein m is 1, 2 or 3, Z is O, C(O) or CH_2;
R^4 and R^5 each independently represent hydrogen, phenyl or a C_{1-6}-alkyl wherein the alkyl group is optionally substituted by one or more phenyl groups;
or a salt thereof.

2. A compound according to claim 1 in which R^1 is C_{1-4}-alkyl, C_{4-8}-cycloalkyl or a phenyl group optionally substituted by one or more halogen atoms or by a CF_3 group.

3. A compound according to claim 1 or 2 in which R^2 is C_{1-6}-alkyl optionally substituted by phenyl or C_{1-6}-thioalkyl or R^2 is a C_{3-8}-cycloalkyl group optionally substituted by phenyl.

4. A compound according to any one of claims 1 to 3 in which X is OH or NHR^3 where R^3 is hydrogen or C_{1-6}-alkyl substituted by hydroxy and optionally by $C(O)NH_2$ or di-fluoro; C_{1-6}-alkyl substituted by $C(O)NH_2$; C_{1-6}-alkyl substituted by C(O)NHMe; C_{1-6}-alkyl substituted by hydroxyphenyl and optionally by $C(O)NR^4R^5$ or R^3 is a lactam ring of formula:



5. A compound according to claim I which is:
[1*S*-(1α,2β,3β,4α)]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(trans)]]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(trans)]]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)-amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]]-2,3-dihydroxy-4-[7-(2-phenylethylamino)-5-(propylthio)-*3H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-2,3-dihydroxy-4-[7-(2-phenylethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-2,3-dihydroxy-4-[7-[2-(methylthio)ethylamino]-5-(propylthio)-3*H*-1,,2,3-triazolo[4,5-d]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-2,3-dihydroxy-4-[7-[2-(methylthio)ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-[1α,2β,3β,4α(trans)]]-4-[5-(Cyclohexylthio)-7-[2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-d]pyrimidin-3-yl]-2,3dihydroxy-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(trans)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(cyclohexylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(3,4-dichlorophenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(phenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(phenylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[*1S-(1α,2β,3β,4α)]-4-*[7-(Cyclopropylamino)-5-(3,4-dichlorophenylthio)-3H-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(3-hydroxy-2,2-difluoropropyl)-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(4-hydroxyphenyl)ethyl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α(*S**),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-*N*-(tetrahydro-3-oxo-isoxazol-4-yl)-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α(*R**),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2-oxo-pyrrolidin-3-yl)-cyclopentanecarboxamide,
[1*S*-[1α(*R**),2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2,3-di-oxo-pyrrolidin-3-yl)-cyclopentanecarboxamide,
[1*S*-[1α(*R**),2β,3β,4α]]-*N*-[(Aminocarbonyl)-methyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α(*R**),2β,3β,4α]]-N-[1-(Aminocarbonyl)-2-(4-hydroxyphenyl)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α(*R**),2β,3β,4α]]-*N*-[1-(Aminocarbonyl)-2-(hydroxy)ethyl]-4-[7-(butylamino)-5-[4-(trifluoromethyl)phenylthio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α(1*R**,2*S**),2β,3β,4α]]-*N*-[1-(Amino-carbonyl)-2-(hydroxy)propyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxycyclopentanecarboxamide,
[1S-[1α,2β,3β,4α]]-N-[2-(Aminocarbonyl)ethyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α,2β,3β,4α]]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(methylaminocarbonyl)-ethyl]-cyclopentanecarboxamide,
[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-(cyclobutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclobutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-[[4-(trifluoromethyl)phenyl]thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-[[4-(trifluoromethyl)phenyl]thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-[(3,3,3-trifluoropropyl)thio]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,4-dimethylpentyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,3-dimethylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1,3-dimethylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Ethylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5- *d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(4-Hydroxybutylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopentylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-d]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1S-(1α,2β,3β,4α)]-4-[5-[(4-Bromophenyl)thio]-7-(butylamino)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-[(6-Hydroxyhexyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(*trans*)]]-2,3-Dihydroxy-4-[5-[[4-(trifluoromethyl)phenyl]thio]-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(cyclopentylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1S-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(3-methylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-d]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(1*R**,2*S**)]]-2,3-Dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-[1α(*R**),2β,3β,4α]]-*N*-(3-Amino-3-oxo-2-propyl)-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentylcarboxamide,
[1*S*-[1α(*R**),2β,3β,4α]]-3-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-hydroxy-1-(methylamino)-1-oxo-2-propyl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-(dimethylamino)-3-oxo-propyl]- cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(dimethylamino)-2-oxo-ethyl)- cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[3-oxo-3-[(phenylmethyl)amino]-propyl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-(methylamino)-2-oxo-ethyl)-cyclopentanecarboxamide,
[1*S*-(1α(*R**),2β,3β,4α)]-*N*-[4-Amino-1-(aminocarbonyl)-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-d]pyrimidin-3yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-*N*-[4-Amino-1-[(methylamino)carbonyl]-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α(*R**),2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-3-hydroxy-propyl)-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-(1α(*R**),2β,3β,4α)]-*N*-[1-(Aminocarbonyl)-2-hydroxy-ethyl)-2,3-dihydroxy-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl] - cyclopentanecarboxamide,
1*S*-[1α,2β,3β,4α(1*S**,2*R**)]-*N*-[(Aminocarbonyl)methyl]-2,3-dihydroxy-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-d]pyrimidin-3-yl]-cyclopentanecarboxamide,

[1*S*-(1α(*R**),2β,3β,4α)]-*N*-[(1-Aminocarbonyl)-4-(methylamino)-4-oxo-butyl]-4-[7-(butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-4-[7-[(1-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-(2,3-dihydroxypropyl)-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-hydroxy-2-(4-hydroxyphenyl)-ethyl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[2-hydroxy-2-(3-hydroxyphenyl)-ethyl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(4-hydroxy-3-methoxyphenyl)-methyl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(4-hydroxyphenyl)-methyl]-cyclopentanecarboxamide,

[1*S*-[1α,2β,3β,4α(1*R**,2*S**)]]-2,3-Dihydroxy-*N*-(2-hydroxyethyl)-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,

[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]]-2,3-Dihydroxy-*N*-(2-hydroxyethyl)-4-[7-[(2-phenylcyclopropyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(2-hydroxy-5-nitrophenyl)methyl]-cyclopentanecarboxamide,

[1*S*-[1α,2β,3β,4α(*trans*)]]-2,3-Dihydroxy-*N*-(2-Hydroxyethyl)-4-[5-[[(4-trifluoromethyl)phenyl]thio]-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(3,4-dihydroxyphenyl)methyl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(2-hydroxyphenyl)methyl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy-*N*-[2-hydroxyethyl]-4-[7-[(4-phenylbutyl)amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Cyclopropylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]- 2,3-dihydroxy-*N*-(2-hydroxyethyl)-cyclopentanecarboxamide,

[1*S*-(1α,2β,3β,4α)]-4-[7-(Butylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-*N*-[(3-hydroxyphenyl)methyl]-cyclopentanecarboxamide,
[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxamide,
[1*S*-[1α,2β,3β,4α(1*R**,2*S**)]]-4-[7-[[2-(4-Chlorophenyl)cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]]-2,3-Dihydroxy-4-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(1*S**,2*R**)]]-2,3-Dihydroxy-4-[5-(methylthio)-7-[(2-phenylcyclopropyl)amino]-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxamide,
[1*S*-(1α,2β,3β,4α)]-2,3-Dihydroxy 4-[7-[2-(phenylamino)ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
[1*S*-(1α,2β,3β,4α)]-4-[7-[2-(4-Chlorophenyl)-ethylamino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-2,3-dihydroxy-cyclopentanecarboxylic acid,
[1*S*-[1α,2β,3β,4α(E)]]-2,3-Dihydroxy-4-[7-(3-iodo-prop-2-enylamino)-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl]-cyclopentanecarboxylic acid,
and pharmaceutically acceptable salts thereof.

6. A pharmaceutical composition comprising a compound according to any one of claims 1 to 5 in combination with a pharmaceutically acceptable diluent, adjuvent or carrier.

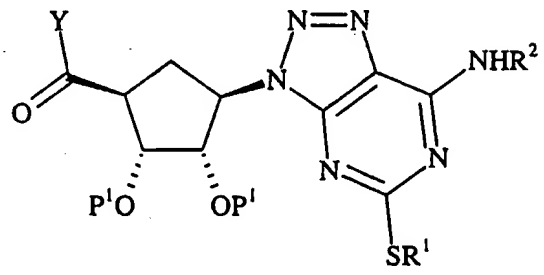
7. A compound according to any one of claims 1 to 5 for use in therapy.

8. Use of a compound according to any one of claims 1 to 5 in the manufacture of a medicament for the treatment of a platelet aggregation disorder.

9. A method for the treatment of a platelet aggregation disorder which comprises administering to a patient suffering from such a disorder a therapeutically effective amount of a compound according to to any one of claims 1 to 5.

10. A process for the preparation of a compound of formula (I) which comprises

(a) deprotecting a compound of formula (II):



(II)

wherein R^1 and R^2 are as defined above, P^1 is a protecting group and Y is X as defined above or O-C_{1-6}-alkyl, O-benzyl or NHR^7 wherein R^7 is a C_{1-6}-alkyl group substituted by a $C(O)OR^8$ group and optionally one or more halogen atoms and/or OR^4, $C(NH)NR^4R^5$, $C(O)NR^4R^5$, phenyl and/or C_{1-6}-alkyl groups, wherein R^4 and R^5 are as defined above and R^8 is C_{1-6}-alkyl or benzyl; and, optionally

(b) reacting the compound of formula (I) thus obtained with a suitable acid or base to prepare a pharmaceutically acceptable salt.

11. A compound of formula (II) as defined in claim 10.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 97/02091

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: C07D 487/04, A61K 31/505, A61K 31/41 // (C07D 487/04, 249:00, 239:00)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: C07D, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, WPI, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 9703084 A1 (ASTRA PHARMACEUTICALS LTD), 30 January 1997 (30.01.97) --	1-11
A	EP 0215759 A1 (REGENTS OF THE UNIVERSITY OF MINNESOTA), 25 March 1987 (25.03.87), the claims --	1-11
A	EP 0368640 A2 (THE WELLCOME FOUNDATION LIMITED), 16 May 1990 (16.05.90), page 11, line 43 - page 12, line 41; the claims --	1-11

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"B" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 February 1998	04.03.1998
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Gerd Strandell Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 97/02091

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 9
because they relate to subject matter not required to be searched by this Authority, namely:

Claim 9 relates to a method of treatment of the human or animal body by surgery or by therapy. See PCT, Rule 39.1.(iv). Nevertheless, a search has been executed for this claim. The search has been based on the alleged effects of the compounds/compositions.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

03/02/98

International application No.
PCT/SE 97/02091

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9703084 A1	30/01/97	AU 6375196 A	10/02/97
		GB 9514074 D	00/00/00
		GB 9520311 D	00/00/00
		GB 9522837 D	00/00/00
EP 0215759 A1	25/03/87	AU 6237686 A	12/03/87
		JP 62142178 A	25/06/87
		US 4742064 A	03/05/88
EP 0368640 A2	16/05/90	JP 2237981 A	20/09/90
		US 5039689 A	13/08/91